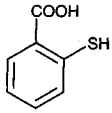
Thiosalicylic acid



Molecular formula: $C_7H_6O_2S$
Molecular weight: 154.19
CAS Registry No.: 147-93-3
Merck Index: 9498

SAMPLE

Matrix: blood, urine
Sample preparation: Plasma. 1 mL Plasma + 50 μL 500 ng/mL mefenamic acid or indomethacin + 1 mL 100 mM HCl + 10 mL dichloromethane, rotate for 10 min, centrifuge at 1500 g for 15 min. Remove the organic layer and evaporate it to dryness under a stream of nitrogen at 45°. Redissolve the residue in mobile phase, inject a 20 μL aliquot. Urine. 50 μL Urine + 1 mL mobile phase, inject a 20 μL aliquot.

HPLC VARIABLES

Column: 75 × 4.6 3 μm Supelcosil LC-8
Mobile phase: MeCN:50 mM phosphoric acid 45:55
Flow rate: 1
Injection volume: 20
Detector: UV 235

CHROMATOGRAM

Retention time: 2.2
Internal standard: mefenamic acid (8) or indomethacin (5)
Limit of detection: 50-250 ng/mL

OTHER SUBSTANCES

Simultaneous: naproxen, flunixin, ethacrynic acid, phenylbutazone

KEY WORDS

plasma

REFERENCE

Singh,A.K.; Jang,Y.; Mishra,U.; Granley,K. Simultaneous analysis of flunixin, naproxen, ethacrynic acid, indomethacin, phenylbutazone, mefenamic acid and thiosalicyclic acid in plasma and urine by high-performance liquid chromatography and gas chromatography-mass spectrometry, *J.Chromatogr.*, **1991**, *568*, 351–361.

SAMPLE

Matrix: formulations
Sample preparation: 9.5 mL Contact lens solution + 0.5 mL 3 mg/mL methylparaben, inject a 20 μL aliquot.

HPLC VARIABLES

Guard column: 7 μm Nucleosil C18 pre-column
Column: 7 μm Nucleosil C18
Mobile phase: MeOH:100 mM KH_2PO_4 adjusted to pH 3.5 with phosphoric acid 60:40
Flow rate: 1
Injection volume: 20
Detector: UV 254

CHROMATOGRAM

Retention time: 10.9
Internal standard: methyl paraben (7.8)

OTHER SUBSTANCES

Simultaneous: chlorhexidine gluconate, thimerosal

Interfering: 2,2-dithisalicylic acid

KEY WORDS
contact lens solutions

REFERENCE
Hu,O.Y.-P.; Wang,S.-Y.; Fang,Y.-J.; Chen,Y.-H.; King,M.-L. Simultaneous determination of thimerosal and chlorhexidine in solutions for soft contact lenses and its applications in stability studies, *J.Chromatogr.*, **1990**, *523*, 321–326.

SAMPLE
Matrix: formulations
Sample preparation: Inject directly or extract as follows. Condition a Sep-Pak C18 SPE cartridge with MeOH and water. 10 mL Ophthalmic solution + 100 µL concentrated phosphoric acid, add to the SPE cartridge, wash with 5 mL water, wash with 2 mL MeOH:water 20:80, elute with 2 mL MeOH, dilute the eluate to 10 mL with MeOH, inject an aliquot.

HPLC VARIABLES
Column: 150 × 4 5 µm Spherisorb C18
Mobile phase: MeOH:water 50:50 containing 2 mM tetraethylammonium perchlorate, adjusted to pH 4.8 with perchloric acid
Flow rate: 1
Injection volume: 20
Detector: E, Metrohm Model 461, Metrohm Model 656 flow cell, carbon paste electrode, 0.9 V

CHROMATOGRAM
Retention time: 3
Limit of detection: 30 ng/mL

OTHER SUBSTANCES
Simultaneous: 2,2'-dithiodibenzoic acid, thimerosal

KEY WORDS
ophthalmic solutions; SPE

REFERENCE
del Pilar da Silva,M.; Procopio,J.R.; Hernández,L. Evaluation of the capability of different chromatographic systems for the monitoring of thimerosal and its degradation products by high-performance liquid chromatography with amperometric detection, *J.Chromatogr.A*, **1993**, *653*, 267–273.

SAMPLE
Matrix: solutions

HPLC VARIABLES
Column: 10 µm Spherisorb 10 ODS
Mobile phase: MeOH:water:phosphoric acid 60:50:1
Flow rate: 2.6
Injection volume: 25
Detector: UV 222

CHROMATOGRAM
Retention time: 3
Limit of detection: 200 ng/mL

OTHER SUBSTANCES
Simultaneous: 2,2'-dithiosalicylic acid, thimerosal

REFERENCE
Reader,M.J.; Lines,C.B. Decomposition of thimerosal in aqueous solution and its determination by high-performance liquid chromatography, *J.Pharm.Sci.*, **1983**, *72*, 1406–1409.

SAMPLE
Matrix: solutions

HPLC VARIABLES
Column: 210 × 4.6 5 μm Spherisorb RP-18
Mobile phase: MeOH:water:phosphoric acid 65:35:0.9
Flow rate: 0.6
Injection volume: 20
Detector: UV 222

CHROMATOGRAM
Retention time: 5.8
Limit of quantitation: 0.15 ppm

OTHER SUBSTANCES
Simultaneous: degradation products, dithiosalicylic acid, thimerosal

REFERENCE
Caraballo,I.; Rabasco,A.M.; Fernández-Arévalo,M. Study of thimerosal degradation mechanism, *Int.J.Pharm.*, **1993**, *89*, 213–221.

SAMPLE
Matrix: solutions

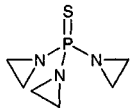
HPLC VARIABLES
Column: 250 × 4.6 Zorbax RX
Mobile phase: Gradient. A was 10 mL concentrated orthophosphoric acid and 7 mL triethylamine in 1 L water. B was 10 mL concentrated orthophosphoric acid and 7 mL triethylamine in 200 mL water, make up to 1 L with MeCN. A:B from 100:0 to 0:100 over 30 min, maintain at 0:100 for 5 min.
Column temperature: 30
Flow rate: 2
Detector: UV 210

OTHER SUBSTANCES
Also analyzed: acepromazine, acetaminophen, acetophenazine, albuterol, aminophylline, amitriptyline, amobarbital, amoxapine, amphetamine, amylocaine, antipyrine, aprobarbital, aspirin, atenolol, atropine, avermectin, barbital, benzocaine, benzoic acid, benzotropine, benzphetamine, berberine, bibucaine, bromazepan, brompheniramine, buprenorphine, buspirone, butabarbital, butacaine, butethal, caffeine, carbamazepine, carbromal, chloramphenicol, chlordiazepoxide, chloroquine, chlorothiazide, chloroxylenol, chlorphenesin, chlorpheniramine, chlorpromazine, chlorpropamide, chlortetracycline, cimetidine, cinchonidine, cinchonine, clenbuterol, clonazepam, clonixin, clorazepate, cocaine, codeine, colchicine, cortisone, coumarin, cyclazocine, cyclobenzaprine, cyclothiazide, cyheptamide, cymarin, danazol, danthron, dapsone, debrisoquine, desipramine, dexamethasone, dextromethorphan, dextropropoxyphene, diamorphine, diazepam, diclofenac, diethylpropion, diethylstilbestrol, diflunisal, digitoxin, digoxin, diltiazem, diphenhydramine, diphenoxylate, diprenorphine, dipyrone, disulfiram, dopamine, doxapram, doxepin, dronabinol, ephedrine, epinephrine, epinine, estradiol, estriol, estrone, ethacrynic acid, ethosuximide, etonitazene, etorphine, eugenol, famotidine, fenbendazole, fencamfamine, fenoprofen, fenproporex, fentanyl, flubendazole, flufenamic acid, flunitrazepam, 5-fluorouracil, fluoxymesterone, fluphenazine, furosemide, gentisic acid, gitoxigenin, glipizide, glunixin, glutethimide, glybenclamide, guaiacol, halazepam, haloperidol, hydrochlorothiazide, hydrocodone, hydrocortisone, hydromorphone, hydroxyquinoline, ibogaine, ibuprofen, iminostilbene, imipramine, indomethacin, isocarbostyril, isocarboxazid, isoniazid, isoproterenol, isoxsuprine, ivermectin, ketamine, ketoprofen, kynurenic acid, levorphanol, lidocaine, lorazepam, lormetazepam, loxapine, mazindol, mebendazole, meclizine, meclofenamic acid, medazepam, mefenamic acid, megestrol, mepacrine, meperidine, mephentermine, mephenytoin, mephesin, mephobarbital, mepivacaine, mescaline, mesoridazine, methadone, methamphetamine, methapyrilene, methaqualone, methazolamide, methocarbamol, methoxamine, methsuximide, methyl salicylate, methyldopa, methyldopamine, methylphenidate, methylprednisolone, methyltestosterone, methyprylon, metoprolol, mibolerone, morphine, nadolol, nalorphine, naloxone, naltrexone, naphazoline, naproxen, nefopam, niacinamide, nicotine, niacin, nifedipine, niflumic

acid, nitrazepam, norepinephrine, nortriptyline, noscapine, nylidrin, oxazepam, oxycodone, oxymorphone, oxyphenbutazone, oxytetracycline, papaverine, pargyline, pemoline, pentazocine, pentobarbital, persantine, phenacetin, phenazocine, phenazopyridine, phencyclidine, phendimetrazine, phenelzine, pheniramine, phenobarbital, phenothiazine, phensuximide, phentermine, phenylbutazone, phenylephrine, phenylpropanolamine, piperocaine, prazepam, prednisolone, primidone, probenecid, progesterone, propiomazine, propranolol, propylparaben, pseudoephedrine, puromycin, pyrilamine, pyrithyldione, quazepam, quinaldic acid, quinidine, quinine, ranitidine, recinnamine, reserpine, resorcinol, saccharin, albuterol, salicylamide, salicylic acid, scopolamine, scopoletin, secobarbital, strychnine, sulfacetamide, sufadiazine, sulfadimethoxine, sulfaethidole, sulfamerazine, sulfamethazine, sulfamethoxizole, sulfanilamide, sulfapyridine, sulfasoxizole, sulindac, tamoxifen, temazepam, testosterone, tetracaine, tetracycline, tetramisole, thebaine, theobromine, theophylline, thiabendazole, thiamine, thiamylal, thiobarbituric acid, thiothixene, thymol, tolazamide, tolazoline, tobutamide, tolmetin, tranylcypromine, triamcinolone, tribenzylamine, trichloromethiazide, trifluoperazine, trihexyphenidyl, trimethoprim, tripelennamine, triprolidine, tropacocaine, tyramine, verapamil, vincamine, warfarin, yohimbine, zoxazolamine

REFERENCE
Hill,D.W.; Kind,A.J. Reversed-phase solvent gradient HPLC retention indexes of drugs, *J.Anal.Toxicol.*, **1994**, *18*, 233–242.

Thiotepa



Molecular formula: $C_6H_{12}N_3PS$
Molecular weight: 189.22
CAS Registry No.: 52-24-4
Merck Index: 9805

SAMPLE
Matrix: blood
Sample preparation: 1 mL Plasma + 2.2 mL water, add 3 mL to an Extrelut 3 SPE cartridge, let stand for 15 min, elute with chloroform. Collect the first 8 mL of effluent, evaporate to dryness under a stream of nitrogen at 20°, reconstitute the residue in 500 µL 1-propanol. Remove a 100 µL aliquot and add 10 µL reagent, heat at 80° for 30 min, cool in an ice bath, add 400 µL taurine solution, add 400 µL OPA solution, let stand for 10 min, inject a 20 µL aliquot. (Reagent was prepared by mixing equal volumes of 80 mM sodium sulfide solution and 100 mM disodium EDTA, prepare fresh daily. Taurine solution was 0.2 mM taurine in 100 mM pH 8.0 phosphate buffer. OPA solution was 0.3 mM o-phthalaldehyde in 100 mM pH 8.0 phosphate buffer.)

HPLC VARIABLES
Column: 250 × 4 5 µm LiChrosorb RP-18
Mobile phase: MeCN:100 mM pH 5.7 phosphate buffer 28:72
Flow rate: 1
Injection volume: 20
Detector: F ex 340 em 440

CHROMATOGRAM
Retention time: 17.0
Limit of detection: 10 mg/mL

OTHER SUBSTANCES
Extracted: metabolites, TEPA

KEY WORDS
rabbit; plasma; SPE; derivatization; pharmacokinetics

REFERENCE
Sano,A.; Matsutani,S.; Takitani,S. High-performance liquid chromatography of the anti-tumour agent triethylenethiophosphoramide and its metabolite triethylenephosphoramide with sodium sulphide, taurine and o-phthalaldehyde as pre-column fluorescent derivatization reagents, *J.Chromatogr.*, **1988**, *458*, 295–301.

SAMPLE
Matrix: blood
Sample preparation: Condition a Bond Elut C18 SPE cartridge with 10 mL MeOH and 10 mL water. Add 1 mL plasma to the SPE cartridge, wash with 10 mL water, wash with 1 mL MeCN: water 20:80, elute with 1 mL MeCN. Evaporate the eluate to dryness under a stream of nitrogen at room temperature, reconstitute the residue in 500 μL 20% MeCN, filter (0.22 μm), inject a 100 μL aliquot. (Use preservative-free heparin when collecting blood.)

HPLC VARIABLES
Column: 250 × 4.6 5 μm Spherisorb ODS II
Mobile phase: MeCN:water 20:80
Flow rate: 1
Injection volume: 100
Detector: UV 200

CHROMATOGRAM
Retention time: 11.4
Limit of quantitation: 25 ng/mL

KEY WORDS
plasma; SPE; pharmacokinetics

REFERENCE
Tinsley,P.W.; O'Dwyer,P.J.; LaCreta,F.P. High-performance liquid chromatographic analysis of N,N',N"-triethylenethiophosphoramide in human plasma, *J.Chromatogr.*, **1989**, *495*, 318–323.

SAMPLE
Matrix: formulations
Sample preparation: Dilute sample with water.

HPLC VARIABLES
Column: 300 × 4.6 5 μm Spherisorb CN5
Mobile phase: MeOH:water 18:82
Flow rate: 1.2
Injection volume: 10
Detector: UV 216

CHROMATOGRAM
Retention time: 6.2

KEY WORDS
injections; stability-indicating

REFERENCE
Xu,Q.A.; Trissel,L.A.; Zhang,Y.; Martinez,J.F.; Gilbert,D.L. Stability of thiotepa (lyophilized) in 5% dextrose injection at 4 and 23°C, *Am.J.Health-Syst.Pharm.*, **1996**, *53*, 2728–2730.

SAMPLE
Matrix: formulations
Sample preparation: Reconstitute thiotepa injection with water to a thiotepa concentration of 10 mg/mL. Filter through a 0.22 μm filter. Dilute with 5% dextrose injection to a thiotepa concentration of 500 μg/mL or 5 mg/mL. Dilute a 5 mg/mL solution 10-fold with water. Inject a 10 μL aliquot. Inject a 10 μL aliquot of the 500 μL/mL solution directly.

HPLC VARIABLES
Column: 300 × 4.6 5 μm Spherisorb CN5 (Alltech)

Mobile phase: MeOH:water 18:82
Flow rate: 1.2
Injection volume: 10
Detector: UV 216

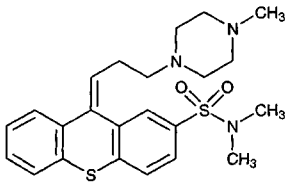
CHROMATOGRAM
Retention time: 6.2

OTHER SUBSTANCES
Simultaneous: degradation products

KEY WORDS
injections; stability-indicating

REFERENCE
Xu,Q.A.; Trissel,L.A.; Zhang,Y.; Martinez,J.F.; Gilbert,D.L. Stability of thiotepa (lyophilized) in 5% dextrose injection at 4 and 23°C, *Am.J.Health-Syst.Pharm.*, **1996**, *53*, 2728–2730.

Thiothixene



Molecular formula: $C_{23}H_{29}N_3O_2S_2$
Molecular weight: 443.63
CAS Registry No.: 5591-45-7, 22189-31-7 (HCl dihydrate), 49746-09-0 (Z HCl dihydrate), 58513- 59-0 (HCl), 49746-04-5 (Z HCl)
Merck Index: 9503
Lednicer No.: 1 400

SAMPLE
Matrix: blood
Sample preparation: 10 mL Plasma or whole blood + 1 mL 1 M NaOH, extract twice with 10 mL hexane for 30 min. Remove the organic layers and evaporate them to dryness under a stream of nitrogen, reconstitute the residue in 1 mL 100 mM HCl, add 5 mL chloroform, vortex for 1 min, centrifuge. Remove a 4.5 mL aliquot of the organic layer and evaporate it to dryness, reconstitute the residue in 100 μL mobile phase, inject a 50 μL aliquot. (It is implied, but not explicitly stated in the paper, that this extraction procedure works for this compound.)

HPLC VARIABLES
Column: 10 μm Micropak CN (Varian)
Mobile phase: MeCN:20 mM ammonium acetate 90:10
Flow rate: 2.5
Injection volume: 50
Detector: UV 254

CHROMATOGRAM
Retention time: 10.0
Limit of detection: 10 ng/mL

OTHER SUBSTANCES
Simultaneous: acetophenazine, amitriptyline, benztropine, butaperazine, carphenazine, chlorpromazine, fluphenazine, haloperidol, mesoridazine, nortriptyline, orphenadrine, piperacetazine, promethazine, thioridazine, trifluoperazine, triflupromazine, trihexyphenidyl, trimeprazine
Interfering: promazine, imipramine

KEY WORDS
plasma; whole blood

REFERENCE

Curry,S.H.; Brown,E.A.; Hu,O.Y.-P.; Perrin,J.H. Liquid chromatographic assay of phenothiazine, thioxanthene and butyrophenone neuroleptics and antihistamines in blood and plasma with conventional and radial compression columns and UV and electrochemical detection, *J.Chromatogr.*, **1982**, *231*, 361–376.

SAMPLE

Matrix: blood

Sample preparation: 2 mL Plasma + 100 μL 1 μg/mL loxapine in isopropanol:diethylamine 99.9:0.1 + 250 μL 25% potassium carbonate containing 0.1% diethylamine + 5 mL hexane: isoamyl alcohol 97:3, vortex for 30 s, centrifuge at 500 g for 3 min. Remove the organic layer and add it to 100 μL 250 mM HCl, vortex for 30 s, inject a 50 μL aliquot of the aqueous phase.

HPLC VARIABLES

Guard column: 50 × 4.6 40 μm C8 (Supelco)
Column: 250 × 4.6 5 μm Supelcosil C8
Mobile phase: MeCN:water:diethylamine:85% phosphoric acid 53.3:45.1:1:0.4, pH adjusted to 7.2 with NaOH or phosphoric acid
Flow rate: 2
Injection volume: 50
Detector: UV 254

CHROMATOGRAM

Retention time: k' 3.39
Internal standard: loxapine (k' 7.18)

OTHER SUBSTANCES

Extracted: amitriptyline, chlordiazepoxide, chlorpromazine, desipramine, desmethldiazepam, desmethylchlordiazepoxide, desmethyldoxepin, diazepam, doxepin, fluphenazine, haloperidol, imipramine, oxazepam, thiothixene
Noninterfering: molindone, perphenazine, trifluoperazine
Interfering: haloperidol, nortriptyline

KEY WORDS

plasma

REFERENCE

Kiel,J.S.; Abramson,R.K.; Morgan,S.L.; Voris,J.C. A rapid high performance liquid chromatographic method for the simultaneous measurement of six tricyclic antidepressants, *J.Liq.Chromatogr.*, **1983**, *6*, 2761–2773.

SAMPLE

Matrix: blood

Sample preparation: 1 mL Plasma + 10 μL 10 μg/mL trans-thiothixene in water + 1 mL 2 M pH 9.8 sodium carbonate + 5 mL hexane:isoamyl alcohol 98.5:1.5, vortex twice for 15 s each time, centrifuge at 700 g for 15 min. Remove the organic layer and evaporate it to dryness under a stream of nitrogen, reconstitute the residue in 50 μL mobile phase, vortex for 15 s, centrifuge for 5 min, inject a 20 μL aliquot.

HPLC VARIABLES

Column: 150 × 4.6 5 μm Spherisorb cyanopropyl
Mobile phase: MeCN:MeOH:10 mM pH 7.0 KH_2PO_4 48:12:40
Flow rate: 2
Injection volume: 20
Detector: UV 229

CHROMATOGRAM

Retention time: 3
Internal standard: trans-thiothixene (4)
Limit of detection: 0.5 ng/mL

OTHER SUBSTANCES

Simultaneous: metabolites amitriptyline, amoxapine, benztropine, chlordiazepoxide, chlorohaloperidol, chlorpromazine, clozapine, desipramine, desmethyldiazepam, desmethyldoxepin, diazepam, doxepin, fluphenazine, flurazepam, haloperidol, imipramine, loxapine, maprotiline, mesoridazine, nortriptyline, protriptyline, thioproperazine, thioridazine, trazodone, trimipramine

KEY WORDS

plasma

REFERENCE

Narasimhachari,N.; Dorey,R.C.; Landa,B.L.; Friedel,R.O. Improved high-performance liquid chromatographic method for the quantitation of cis-thiothixene in plasma samples using trans-thiothixene as internal standard, *J.Chromatogr.*, **1984**, *311*, 424–429.

SAMPLE

Matrix: blood

Sample preparation: 1 mL Plasma + 100 μL 100 ng/mL trifluoperazine dihydrochloride in 50 mM HCl + 200 μL concentrated ammonium hydroxide + 7 mL n-pentane:isopropanol 95:5, shake horizontally for 30 min, centrifuge at 2000 g. Remove the top organic layer and add it to 2 mL 100 mM perchloric acid, agitate for 10 min, centrifuge. Remove the aqueous layer and add it to 200 μL concentrated ammonium hydroxide, add 6 mL n-pentane:isopropanol 95:5, agitate for 30 min, centrifuge. Remove the top organic layer and evaporate it to dryness under a stream of nitrogen at 45°, reconstitute the residue in 50 μL MeCN, inject a 20-40 μL aliquot. (Clean glassware scrupulously by soaking overnight in 50 mL/L Contrad (Curtin Matheson), rinse several times with water, and air dry.)

HPLC VARIABLES

Column: 250 × 4.6 5 μm Ultrasphere cyano

Mobile phase: MeCN:10 mM pH 2.5 KH_2PO_4 60:40

Flow rate: 2.5

Injection volume: 20-40

Detector: E, Environmental Science Associates Coulochem Model 5100A, Model 5100 guard cell +0.85 V (between pump and injector), Model 5010 analytical cell +0.8 V, preanalytical cell +0.3 V

CHROMATOGRAM

Retention time: 6.4

Internal standard: trifluoperazine dihydrochloride (8.2)

Limit of detection: 0.2 ng/mL

OTHER SUBSTANCES

Simultaneous: amitriptyline, amoxapine, chlorpromazine, desipramine, doxepin, haloperidol, imipramine, loxapine, mesoridazine, nortriptyline, pheniramine, phenylephrine, prochlorperazine, promazine, promethazine, trazodone, trimeprazine, tripelennamine

Noninterfering: diazepam, diphenhydramine, ethopropazine, fluoxetine, nordiazepam, oxazepam, phenylpropanolamine, pseudoephedrine

Interfering: fluphenazine, perphenazine, thioridazine, triflupromazine

KEY WORDS

plasma

REFERENCE

Hariharan,M.; VanNoord,T.; Kindt,E.K.; Tandon,R. A simple, sensitive liquid chromatographic assay of cis-thiothixene in plasma with coulometric detection, *Ther.Drug Monit.*, **1991**, *13*, 79–85.

SAMPLE

Matrix: blood

Sample preparation: Condition a 3 mL Bond Elut Certify SPE cartridge with 2 mL MeOH and 2 mL 100 mM pH 6.0 phosphate buffer, do not allow to dry. 1 mL Whole blood + 6 mL 100 mM pH 6.0 phosphate buffer, vortex, sonicate, centrifuge, add the supernatant to the SPE cartridge,

wash with water, wash with 1 mM pH 3.3 acetic acid, dry under suction, wash with 2 mL acetone:chloroform 50:50, elute with 3 mL freshly prepared ethyl acetate:ammonia 98:2. Evaporate the eluate under a stream of nitrogen at 40°, reconstitute in 50 μL MeOH, inject a 10 μL aliquot.

HPLC VARIABLES

Column: 125 × 4 5 μm Asahipak ODP-50
Mobile phase: MeCN:50 mM ammonium acetate 85:15
Flow rate: 0.6
Injection volume: 10
Detector: MS, Finnigan MAT TSQ 700 tandem quadrupole, Finnigan MAT TSP-2 interface, collision gas argon 2.5 mTorr, collision offset -15 V, repeller 70 V, vaporizer 130-5°, source 200°, filament off, multiplier 1500 V, dynode power 15 kV, scantime 1.20 s, MSMSC factor 0, monitor 444–335. (The effluent from the column was mixed with 50 mM ammonium acetate pumped at 0.6 mL/min. The mixture flowed to the detector.)

CHROMATOGRAM

Retention time: 2.50
Limit of detection: 5 ng

OTHER SUBSTANCES

Extracted: chlorprothixene, flupenthixol, zuclopenthixol

KEY WORDS

whole blood; SPE

REFERENCE

Verweij,A.M.A.; Hordijk,M.L.; Lipman,P.J.L. Quantitative liquid chromatography, thermospray/tandem mass spectrometric (LC/TSP/MS/MS) analysis of some tranquilizers of the thioxanthene group in whole-blood, *J.Liq.Chromatogr.*, **1994**, *17*, 4009–4110.

SAMPLE

Matrix: blood, tissue
Sample preparation: Blood or serum. 1 mL Blood or serum + 1 μg cianopramine + 1 mL water, vortex, add 1 mL 200 mM sodium carbonate, vortex, add 6 mL hexane:1-butanol 95:5, gently agitate for 30 min, centrifuge at 2500 g for 5 min. Remove the organic layer and add it to 100 μL 0.2% phosphoric acid, agitate gently for 30 min, centrifuge for 5 min. Remove the organic layer and inject a 30 μL aliquot of the aqueous layer. Liver homogenate. 0.5 mL Liver homogenate + 10 μg cianopramine + 500 μL 2% sodium tetraborate + 8 mL hexane:1-butanol 95:5, gently agitate for 30 min, centrifuge at 2500 g for 5 min. Remove the organic layer and add it to 400 μL 0.2% phosphoric acid, agitate gently for 30 min, centrifuge for 5 min. Remove the organic layer and inject a 30 μL aliquot of the aqueous layer.

HPLC VARIABLES

Guard column: 15 × 3.2 7 μm RP-18 Newguard (Applied Biosystems)
Column: 100 × 4.6 5 μm Brownlee Spheri-5 RP-18
Mobile phase: MeCN:100 mM NaH_2PO_4:diethylamine 40:57.5:2.5
Flow rate: 2
Injection volume: 30
Detector: UV 220

CHROMATOGRAM

Retention time: 17.62
Internal standard: cianopramine (8.93)

OTHER SUBSTANCES

Simultaneous: amitriptyline, amoxapine, benztropine, brompheniramine, chlorpheniramine, chlorpromazine, clomipramine, cyproheptadine, desipramine, diphenhydramine, dothiepin, doxepin, fluoxetine, haloperidol, imipramine, loxapine, maprotiline, meperidine, mesoridazine, methadone, metoclopramide, mianserin, moclobemide, nomifensine, nordoxepin, norfluoxetine, norpropoxyphene, northiaden, nortriptyline, pentobarbital, pheniramine, promethazine, propoxyphene, propranolol, protriptyline, quinidine, quinine, sulforidazine, thioridazine, tranylcypromine, trazodone, trihexyphenidyl, trimipramine, triprolidine

Noninterfering: dextromethorphan, norphetidine, phenoxybenzamine, prochlorperazine, trifluoperazine

KEY WORDS
serum; whole blood; liver

REFERENCE
McIntyre,I.M.; King,C.V.; Skafidis,S.; Drummer,O.H. Dual ultraviolet wavelength high-performance liquid chromatographic method for the forensic or clinical analysis of seventeen antidepressants and some selected metabolites, *J.Chromatogr.*, **1993**, *621*, 215–223.

SAMPLE
Matrix: bulk, formulations
Sample preparation: Capsules. Shake the contents of a capsule with mobile phase for 30 min, make up to 100 mL with mobile phase, filter, dilute as necessary with mobile phase, inject an aliquot. Bulk. Prepare a 30-35 μg/mL aliquot in mobile phase, inject an aliquot.

HPLC VARIABLES
Column: 100 × 4.6 5 μm SiAl (ES Industries)
Mobile phase: MeCN:water:buffer 60:20:20 (Buffer was 3.15 g $LiOH.H_2O$ in 950 mL water, adjusted to pH 5.5 ± 0.05 with phosphoric acid, and made up to 1 L with water.) (A column of 18 μm silica (Supelco 5-8411) was placed between the pump and the injection valve.)
Flow rate: 3
Injection volume: 10
Detector: UV 225

CHROMATOGRAM
Retention time: 1.7

OTHER SUBSTANCES
Simultaneous: E-thiothixene, impurities

KEY WORDS
capsules; stability-indicating

REFERENCE
Severin,G. Comprehensive high-performance liquid chromatographic methodology for the determination of thiothixene in bulk drug, finished product, and dissolution testing samples, *J.Pharm.Sci.*, **1987**, *76*, 231–234.

SAMPLE
Matrix: solutions
Sample preparation: Make up a solution in mobile phase, inject a 20 μL aliquot.

HPLC VARIABLES
Column: 100 × 3 5 μm Lichrosorb SI60
Mobile phase: MeCN:MeOH:ammonium hydroxide 250:55:13
Flow rate: 1.2
Injection volume: 20
Detector: UV 240

CHROMATOGRAM
Retention time: 3.5
Internal standard: perazine (5)

OTHER SUBSTANCES
Simultaneous: N-acetylprocainamide, butaperazine, chlorimipramine, chlorpromazine, codeine, desipramine, dimethacrine, diphenhydramine, disopyramide, doxepin, hydroquinidine, maprotiline, melitracene, mesoridazine, nortriptyline, opipramol, perphenazine, procainamide, prochlorperazine, promazine, prothipendyl, protriptyline, quinidine, thioperazine, thioridazine, trifluoperazine

Noninterfering: acenocoumaron, acetaminophen, acetophenetidine, aspirin, benzodiazepines, bibenzepin, butriptyline, caffeine, chlorprothixene, clopenthixol, clothiapine, dixyrazine, droperidol, fluphenazine, haloperidol, hydroxyzine, isoniazid, methotrimeprazine, metopimazine, moperone, noxiptyline, orphenadrine, pericyazine, phenprocoumon, pipothiazine, promethazine, salicylic acid, theophylline, thiopropazate, trimeprazine, trimipramine
Interfering: imipramine, pipamperone, thiethylperazine, amitriptyline

KEY WORDS
maprotiline prevents adsorption on glass

REFERENCE
Edelbroek,P.M.; de Haas,E.J.M.; de Wolff,F.A. Liquid-chromatographic determination of amitryptyline and its metabolites in serum, with adsorption onto glass minimized, *Clin.Chem.*, **1982**, *28*, 2143–2148.

SAMPLE
Matrix: solutions
Sample preparation: Prepare a 10 μg/mL solution in MeOH, inject a 20 μL aliquot.

HPLC VARIABLES
Column: 125 × 4.9 Spherisorb S5W silica
Mobile phase: MeOH containing 10 mM ammonium perchlorate and 1 mL/L 100 mM NaOH in MeOH, pH 6.7
Flow rate: 2
Injection volume: 20
Detector: E, LeCarbone, V25 glassy carbon electrode, + 1.2 V

CHROMATOGRAM
Retention time: 4.3

OTHER SUBSTANCES
Also analyzed: acebutolol, acepromazine, acetophenazine, N-acetylprocainamide, albuterol, alprenolol, amethocaine, amiodarone, amitriptyline, antazoline, atenolol, azacyclonal, bamethan, benactyzine, benperidol, benzethidine, benzocaine, benzoctamine, benzphetamine, benzquinamide, bromhexine, bromodiphenhydramine, bromperidol, brompheniramine, brompromazine, buclizine, bufotenine, bupivacaine, buprenorphine, butacaine, butethamate, chlorcyclizine, chlorpheniramine, chlorphenoxamine, chlorprenaline, chlorpromazine, chlorprothixene, cimetidine, cinchonidine, cinnarizine, clemastine, clomipramine, clonidine, cocaine, cyclazocine, cyclizine, cyclopentamine, cyproheptadine, deserpidine, desipramine, dextromoramide, dextropropoxyphene, dicyclomine, diethylcarbamazine, diethylpropion, diethylthiambutene, dihydroergotamine, dimethindene, dimethothiazine, diphenhydramine, diphenoxylate, dipipanone, diprenorphine, dipyridamole, disopyramide, dothiepin, doxapram, doxepin, doxylamine, droperidol, ephedrine, ergocornine, ergocristine, ergocristinine, ergocryptine, ergometrine, ergosine, ergosinine, ergotamine, ethopropazine, etorphine, etoxeridine, fenethazine, fenfluramine, fenoterol, fentanyl, flavoxate, fluopromazine, flupenthixol, fluphenazine, flurazepam, haloperidol, hydroxyzine, hyoscine, ibogaine, imipramine, indapamine, iprindole, isothipendyl, isoxsuprine, ketanserin, laudanosine, lidocaine, lofepramine, loxapine, maprotiline, mecamylamine, meclophenoxate, meclozine, medazepam, mephentermine, mepivacaine, meptazinol, mepyramine, mesoridazine, metaraminol, methadone, methamphetamine, methapyrilene, methdilazene, methotrimeprazine, methoxamine, methoxyphenamine, methoxypromazine, methylephedrine, methylergonovine, methysergide, metoclopramide, metopimazine, metoprolol, mianserin, morazone, nadolol, nalorphine, naloxone, naphazoline, nicotine, nifedipine, nomifensine, nortriptyline, noscapine, orphenadrine, oxeladin, oxprenolol, oxymetazolin, papaverine, pargyline, pecazine, penbutolol, pentazocine, penthienate, pericyazine, perphenazine, phenadoxone, phenampromide, phenazocine, phenbutrazate, phendimetrazine, phenelzine, phenglutarimide, phenindamine, pheniramine, phenmetrazine, phenomorphan, phenoperidine, phenothiazine, phenoxybenzamine, phentolamine, phenylephrine, phenyltoloxamine, physostigmine, piminodine, pimozide, pindolol, pipamazine, pipazethate, piperacetazine, piperidolate, pipradol, pirenzepine, piritramide, pizotifen, practolol, pramoxine, prazosin, prenylamine, prilocaine, primaquine, proadifen, procainamide, procaine, prochlorperazine, procyclidine, proheptazine, prolintane, promazine, promethazine, pronethalol, properidine, propiomazine, propranolol, prothipendyl, protriptyline, proxymetacaine, pseudoephedrine, pyrimethamine, quinidine, quinine, ranitidine, rescinnamine, sotalol, tacrine, terazosin, terbutaline, terfenadine, thenyldiamine, theophylline, thiethylperazine, thiopropazate, thioproperazine, thioridazine,

thonzylamine, timolol, tocainide, tolpropamine, tolycaine, tranylcypromine, trazodone, trifluoperazine, trifluperidol, trimeperidine, trimeprazine, trimethobenzamide, trimethoprim, trimipramine, tripelennamine, triprolidine, tryptamine, verapamil, xylometazoline

REFERENCE

Jane,I.; McKinnon,A.; Flanagan,R.J. High-performance liquid chromatographic analysis of basic drugs on silica columns using non-aqueous ionic eluents. II. Application of UV, fluorescence and electrochemical oxidation detection, *J.Chromatogr.*, **1985**, *323*, 191–225.

SAMPLE

Matrix: solutions
Sample preparation: Make up a solution in mobile phase, inject a 120 μL aliquot.

HPLC VARIABLES

Guard column: 15 × 3.2 Alltech RP-18 guard column
Column: 250 × 4.6 5 μm Supelcosil LC18-DB
Mobile phase: MeOH:MeCN:water:1 M ammonium hydroxide 50:35:15:0.3, adjusted to pH 6.7-8.0 with 6 M HCl
Flow rate: 1
Injection volume: 120
Detector: UV 263

CHROMATOGRAM

Retention time: 5.6

OTHER SUBSTANCES

Simultaneous: chlorpromazine, amitriptyline, clozapine, chlordiazepoxide, thioridazine, mesoridazine, sulforidazine, fluoxetine
Noninterfering: flurazepam, methylphenidate, ephedrine
Interfering: desipramine, nortriptyline, imipramine, maprotiline

REFERENCE

Jortani,S.A.; Poklis,A. Determination of thioridazine enantiomers in human serum by sequential achiral and chiral high-performance liquid chromaqtography, *J.Anal.Toxicol.*, **1993**, *17*, 374–377.

SAMPLE

Matrix: solutions

HPLC VARIABLES

Guard column: 30 × 2.1 Spheri-5 RP-8
Column: 220 × 2.1 Spheri-5 RP-8
Mobile phase: Gradient. A was 0.08% diethylamine and 0.09% phosphoric acid in water, pH 2.3. B was MeCN:water 90:10 containing 0.08% diethylamine and 0.09% phosphoric acid. A:B 95:5 for 2 min, to 0:100 over 15 min (?), maintain at 0:100 for 5 min.
Column temperature: 50
Flow rate: 0.5
Detector: UV 200

CHROMATOGRAM

Retention time: 14

OTHER SUBSTANCES

Simultaneous: mesoridazine, promazine, chlorpromazine, trifluoperazine, thioridazine
Also analyzed: amitriptyline, amphetamine, chlordiazepoxide, desalkylflurazepam, desipramine, desmethyldoxepin, diazepam, diethylpropion, doxepin, ephedrine, fenfluramine, flurazepam, imipramine, methamphetamine, norchlordiazepoxide, nordiazepam, nortriptyline, oxazepam, phentermine, phenylpropanolamine, prazepam

REFERENCE

Rainin Catalog, C1-94, **1994**, p. 7.24.

SAMPLE
Matrix: solutions
Sample preparation: Prepare a 1 mg/mL solution in MeOH, inject a 5 μL aliquot.

HPLC VARIABLES
Column: 250 × 4.6 5 μm Lichrosphere cyanopropyl
Mobile phase: Carbon dioxide:MeOH:isopropylamine 94:6:0.03
Column temperature: 50
Flow rate: 3
Injection volume: 5
Detector: UV 254

CHROMATOGRAM
Retention time: 8.3

OTHER SUBSTANCES
Simultaneous: trifluprομazine, carphenazine, methotrimeprazine, promazine, perphenazine, chlorprothixene, deserpidine, reserpine
Also analyzed: acetophenazine, ethopropazine, promethazine, propiomazine

KEY WORDS
SFC; pressure 200 bar

REFERENCE
Berger,T.A.; Wilson,W.H. Separation of drugs by packed column supercritical fluid chromatography. 1. Phenothiazine antipsychotics, *J.Pharm.Sci.*, **1994**, *83*, 281–286.

SAMPLE
Matrix: solutions

HPLC VARIABLES
Column: 250 × 4.6 Zorbax RX
Mobile phase: Gradient. A was 10 mL concentrated orthophosphoric acid and 7 mL triethylamine in 1 L water. B was 10 mL concentrated orthophosphoric acid and 7 mL triethylamine in 200 mL water, make up to 1 L with MeCN. A:B from 100:0 to 0:100 over 30 min, maintain at 0:100 for 5 min.
Column temperature: 30
Flow rate: 2
Detector: UV 210

OTHER SUBSTANCES
Also analyzed: acepromazine, acetaminophen, acetophenazine, albuterol, aminophylline, amitriptyline, amobarbital, amoxapine, amphetamine, amylocaine, antipyrine, aprobarbital, aspirin, atenolol, atropine, avermectin, barbital, benzocaine, benzoic acid, benzotropine, benzphetamine, berberine, bibucaine, bromazepan, brompheniramine, buprenorphine, buspirone, butabarbital, butacaine, butethal, caffeine, carbamazepine, carbromal, chloramphenicol, chlordiazepoxide, chloroquine, chlorothiazide, chloroxylenol, chlorphenesin, chlorpheniramine, chlorpromazine, chlorpropamide, chlortetracycline, cimetidine, cinchonidine, cinchonine, clenbuterol, clonazepam, clonixin, clorazepate, cocaine, codeine, colchicine, cortisone, coumarin, cyclazocine, cyclobenzaprine, cyclothiazide, cyheptamide, cymarin, danazol, danthron, dapsone, debrisoquine, desipramine, dexamethasone, dextromethorphan, dextropropoxyphene, diamorphine, diazepam, diclofenac, diethylpropion, diethylstilbestrol, diflunisal, digitoxin, digoxin, diltiazem, diphenhydramine, diphenoxylate, diprenorphine, dipyrone, disulfiram, dopamine, doxapram, doxepin, dronabinol, ephedrine, epinephrine, epinine, estradiol, estriol, estrone, ethacrynic acid, ethosuximide, etonitazene, etorphine, eugenol, famotidine, fenbendazole, fencamfamine, fenoprofen, fenproporex, fentanyl, flubendazole, flufenamic acid, flunitrazepam, 5-fluorouracil, fluoxymesterone, fluphenazine, furosemide, gentisic acid, gitoxigenin, glipizide, glunixin, glutethimide, glybenclamide, guaiacol, halazepam, haloperidol, hydrochlorothiazide, hydrocodone, hydrocortisone, hydromorphone, hydroxyquinoline, ibogaine, ibuprofen, iminostilbene, imipramine, indomethacin, isocarbostyril, isocarboxazid, isoniazid, isoproterenol, isoxsuprine, ivermectin, ketamine, ketoprofen, kynurenic acid, levorphanol, lidocaine, lorazepam, lormetazepam, loxapine, mazindol, mebendazole, meclizine, meclofenamic acid, medazepam,

mefenamic acid, megestrol, mepacrine, meperidine, mephentermine, mephenytoin, mephesin, mephobarbital, mepivacaine, mescaline, mesoridazine, methadone, methamphetamine, methapyrilene, methaqualone, methazolamide, methocarbamol, methoxamine, methsuximide, methyl salicylate, methyldopa, methyldopamine, methylphenidate, methylprednisolone, methyltestosterone, methyprylon, metoprolol, mibolerone, morphine, nadolol, nalorphine, naloxone, naltrexone, naphazoline, naproxen, nefopam, niacinamide, nicotine, niacin, nifedipine, niflumic acid, nitrazepam, norepinephrine, nortriptyline, noscapine, nylidrin, oxazepam, oxycodone, oxymorphone, oxyphenbutazone, oxytetracycline, papaverine, pargyline, pemoline, pentazocine, pentobarbital, persantine, phenacetin, phenazocine, phenazopyridine, phencyclidine, phendimetrazine, phenelzine, pheniramine, phenobarbital, phenothiazine, phensuximide, phentermine, phenylbutazone, phenylephrine, phenylpropanolamine, piperocaine, prazepam, prednisolone, primidone, probenecid, progesterone, propiomazine, propranolol, propylparaben, pseudoephedrine, puromycin, pyrilamine, pyrithyldione, quazepam, quinaldic acid, quinidine, quinine, ranitidine, recinnamine, reserpine, resorcinol, saccharin, albuterol, salicylamide, salicylic acid, scopolamine, scopoletin, secobarbital, strychnine, sulfacetamide, sufadiazine, sulfadimethoxine, sulfaethidole, sulfamerazine, sulfamethazine, sulfamethoxizole, sulfanilamide, sulfapyridine, sulfasoxizole, sulindac, tamoxifen, temazepam, testosterone, tetracaine, tetracycline, tetramisole, thebaine, theobromine, theophylline, thiabendazole, thiamine, thiamylal, thiobarbituric acid, thioridazine, thymol, tolazamide, tolazoline, tobutamide, tolmetin, tranylcypromine, triamcinolone, tribenzylamine, trichloromethiazide, trifluoperazine, trihexyphenidyl, trimethoprim, tripelennamine, triprolidine, tropacocaine, tyramine, verapamil, vincamine, warfarin, yohimbine, zoxazolamine

REFERENCE

Hill,D.W.; Kind,A.J. Reversed-phase solvent gradient HPLC retention indexes of drugs, *J.Anal.Toxicol.*, **1994**, *18*, 233–242.

SAMPLE

Matrix: solutions

HPLC VARIABLES

Column: 250 × 4.6 5 μm Supelcosil LC-DP (A) or 250 × 4 5 μm LiChrospher 100 RP-8 (B)
Mobile phase: MeCN:0.025% phosphoric acid:buffer 25:10:5 (A) or 60:25:15 (B) (Buffer was 9 mL concentrated phosphoric acid and 10 mL triethylamine in 900 mL water, adjust pH to 3.4 with dilute phosphoric acid, make up to 1 L.)
Flow rate: 0.6
Injection volume: 25
Detector: UV 229

CHROMATOGRAM

Retention time: 16.49 (A), 6.57 (B)

OTHER SUBSTANCES

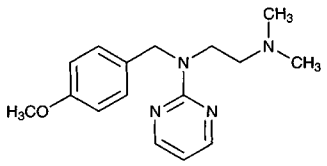
Also analyzed: acebutolol, acepromazine, acetaminophen, acetazolamide, acetophenazine, albuterol, alprazolam, amitriptyline, amobarbital, amoxapine, antipyrine, atenolol, atropine, azatadine, baclofen, benzocaine, bromocriptine, brompheniramine, brotizolam, bupivacaine, buspirone, butabarbital, butalbital, caffeine, carbamazepine, cetirizine, chlorcyclizine, chlordiazepoxide, chlormezanone, chloroquine, chlorpheniramine, chlorpromazine, chlorpropamide, chlorprothixene, chlorthalidone, chlorzoxazone, cimetidine, cisapride, clomipramine, clonazepam, clonidine, clozapine, cocaine, codeine, colchicine, cyclizine, cyclobenzaprine, dantrolene, desipramine, diazepam, diclofenac, diflunisal, diltiazem, diphenhydramine, diphenidol, diphenoxylate, dipyridamole, disopyramide, dobutamine, doxapram, doxepin, droperidol, encainide, ethidium bromide, ethopropazine, fenoprofen, fentanyl, flavoxate, fluoxetine, fluphenazine, flurazepam, flurbiprofen, fluvoxamine, furosemide, glutethimide, glyburide, guaifenesin, haloperidol, homatropine, hydralazine, hydrochlorothiazide, hydrocodone, hydromorphone, hydroxychloroquine, hydroxyzine, ibuprofen, imipramine, indomethacin, ketoconazole, ketoprofen, ketorolac, labetalol, levorphanol, lidocaine, loratadine, lorazepam, lovastatin, loxapine, mazindol, mefenamic acid, meperidine, mephenytoin, mepivacaine, mesoridazine, metaproterenol, metformin, methadone, methdilazine, methocarbamol, methotrexate, methotrimeprazine, methoxamine, methyldopa, methylphenidate, metoclopramide, metolazone, metoprolol, metronidazole, midazolam, moclobemide, morphine, nadolol, nalbuphine, naloxone, naphazoline, naproxen, nifedipine, nizatidine, norepinephrine, nortriptyline, oxazepam, oxycodone, oxymetazoline, paroxetine, pemoline, pentazocine, pentobarbital, pentoxifylline, perphenazine, phen-

iramine, phenobarbital, phenol, phenolphthalein, phentolamine, phenylbutazone, phenyltoloxamine, phenytoin, pimozide, pindolol, piroxicam, pramoxine, prazepam, prazosin, probenecid, procainamide, procaine, prochlorperazine, procyclidine, promazine, promethazine, propafenone, propantheline, propiomazine, propofol, propranolol, protriptyline, quazepam, quinidine, quinine, racemethorphan, ranitidine, remoxipride, risperidone, salicylic acid, scopolamine, secobarbital, sertraline, sotalol, spironolactone, sulfinpyrazone, sulindac, temazepam, terbutaline, terfenadine, tetracaine, theophylline, thiethylperazine, thiopental, thioridazine, timolol, tocainide, tolbutamide, tolmetin, trazodone, triamterene, triazolam, trifluoperazine, triflupromazine, trimeprazine, trimethoprim, trimipramine, verapamil, warfarin, xylometazoline, yohimbine, zopiclone

KEY WORDS
details of plasma extraction

REFERENCE
Koves,E.M. Use of high-performance liquid chromatography-diode array detection in forensic toxicology, *J.Chromatogr.A*, **1995**, *692*, 103–119.

Thonzylamine



Molecular formula: $C_{16}H_{22}N_4O$
Molecular weight: 286.38
CAS Registry No.: 63-56-9
Merck Index: 9513
Lednicer No.: 1 52

SAMPLE
Matrix: solutions
Sample preparation: Prepare a 10 μg/mL solution in MeOH, inject a 20 μL aliquot.

HPLC VARIABLES
Column: 125 × 4.9 Spherisorb S5W silica
Mobile phase: MeOH containing 10 mM ammonium perchlorate and 1 mL/L 100 mM NaOH in MeOH, pH 6.7
Flow rate: 2
Injection volume: 20
Detector: E, LeCarbone, V25 glassy carbon electrode, + 1.2 V

CHROMATOGRAM
Retention time: 3.8

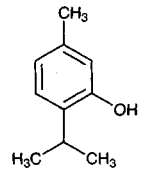
OTHER SUBSTANCES
Also analyzed: acebutolol, acepromazine, acetophenazine, N-acetylprocainamide, albuterol, alprenolol, amethocaine, amiodarone, amitriptyline, antazoline, atenolol, azacyclonal, bamethan, benactyzine, benperidol, benzethidine, benzocaine, benzoctamine, benzphetamine, benzquinamide, bromhexine, bromodiphenhydramine, bromperidol, brompheniramine, brompromazine, buclizine, bufotenine, bupivacaine, buprenorphine, butacaine, butethamate, chlorcyclizine, chlorpheniramine, chlorphenoxamine, chlorprenaline, chlorpromazine, chlorprothixene, cimetidine, cinchonidine, cinnarizine, clemastine, clomipramine, clonidine, cocaine, cyclazocine, cyclizine, cyclopentamine, cyproheptadine, deserpidine, desipramine, dextromoramide, dextropropoxyphene, dicyclomine, diethylcarbamazine, diethylpropion, diethylthiambutene, dihydroergotamine, dimethindene, dimethothiazine, diphenhydramine, diphenoxylate, dipipanone, diprenorphine, dipyridamole, disopyramide, dothiepin, doxapram, doxepin, doxylamine, droperidol, ephedrine, ergocornine, ergocristine, ergocristinine, ergocryptine, ergometrine, ergosine, ergosinine, ergotamine, ethopropazine, etorphine, etoxeridine, fenethazine, fenfluramine, fenoterol, fentanyl, flavoxate, fluopromazine, flupenthixol, fluphenazine, flurazepam, haloperidol, hydroxyzine, hyoscine, ibogaine, imipramine, indapamine, iprindole, isothipendyl, isoxsuprine, ketanserin, laudanosine, lidocaine, lofepramine, loxapine, maprotiline, mecamyl-

amine, meclophenoxate, meclozine, medazepam, mephentermine, mepivacaine, meptazinol, mepyramine, mesoridazine, metaraminol, methadone, methamphetamine, methapyrilene, methdilazene, methotrimeprazine, methoxamine, methoxyphenamine, methoxypromazine, methylephedrine, methylergonovine, methysergide, metoclopramide, metopimazine, metoprolol, mianserin, morazone, nadolol, nalorphine, naloxone, naphazoline, nicotine, nifedipine, nomifensine, nortriptyline, noscapine, orphenadrine, oxeladin, oxprenolol, oxymetazolin, papaverine, pargyline, pecazine, penbutolol, pentazocine, penthienate, pericyazine, perphenazine, phenadoxone, phenampromide, phenazocine, phenbutrazate, phendimetrazine, phenelzine, phenglutarimide, phenindamine, pheniramine, phenmetrazine, phenomorphan, phenoperidine, phenothiazine, phenoxybenzamine, phentolamine, phenylephrine, phenyltoloxamine, physostigmine, piminodine, pimozide, pindolol, pipamazine, pipazethate, piperacetazine, piperidolate, pipradol, pirenzepine, piritramide, pizotifen, practolol, pramoxine, prazosin, prenylamine, prilocaine, primaquine, proadifen, procainamide, procaine, prochlorperazine, procyclidine, proheptazine, prolintane, promazine, promethazine, pronethalol, properidine, propiomazine, propranolol, prothipendyl, protriptyline, proxymetacaine, pseudoephedrine, pyrimethamine, quinidine, quinine, ranitidine, rescinnamine, sotalol, tacrine, terazosin, terbutaline, terfenadine, thenyldiamine, theophylline, thiethylperazine, thiopropazate, thioproperazine, thioridazine, thiothixene, timolol, tocainide, tolpropamine, tolycaine, tranylcypromine, trazodone, trifluoperazine, trifluperidol, trimeperidine, trimeprazine, trimethobenzamide, trimethoprim, trimipramine, tripelennamine, triprolidine, tryptamine, verapamil, xylometazoline

REFERENCE

Jane,I.; McKinnon,A.; Flanagan,R.J. High-performance liquid chromatographic analysis of basic drugs on silica columns using non-aqueous ionic eluents. II. Application of UV, fluorescence and electrochemical oxidation detection, *J.Chromatogr.*, **1985**, *323*, 191–225.

Thymol



Molecular formula: $C_{10}H_{14}O$
Molecular weight: 150.22
CAS Registry No.: 89-83-8, 528-79-0 (acetate)
Merck Index: 9540

SAMPLE

Matrix: solutions

HPLC VARIABLES

Column: 250 × 4 ODS (Hitachi)
Mobile phase: MeCN:50 mM phosphoric acid 50:50 containing 300 mM KCl
Column temperature: 55
Flow rate: 0.6
Injection volume: 20
Detector: UV 272

OTHER SUBSTANCES

Also analyzed: amitriptyline, chlorpromazine, promazine, clomipramine, promethazine

REFERENCE

Sugawara,M.; Takekuma,Y; Yamada,H.; Kobayashi,M.; Iseki,K.; Miyazaki,K. A general approach for the prediction of the intestinal absorption of drugs: regression analysis using the physicochemical properties and drug-membrane electrostatic interactions, *J.Pharm.Sci.*, **1998**, *87*, 960–966.

SAMPLE

Matrix: solutions

HPLC VARIABLES

Column: 250 × 4.6 Zorbax RX

Mobile phase: Gradient. A was 10 mL concentrated orthophosphoric acid and 7 mL triethylamine in 1 L water. B was 10 mL concentrated orthophosphoric acid and 7 mL triethylamine in 200 mL water, make up to 1 L with MeCN. A:B from 100:0 to 0:100 over 30 min, maintain at 0:100 for 5 min.
Column temperature: 30
Flow rate: 2
Detector: UV 210

OTHER SUBSTANCES

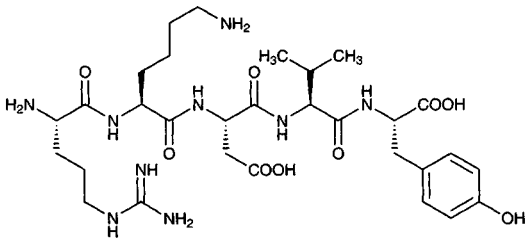
Also analyzed: acepromazine, acetaminophen, acetophenazine, albuterol, aminophylline, amitriptyline, amobarbital, amoxapine, amphetamine, amylocaine, antipyrine, aprobarbital, aspirin, atenolol, atropine, avermectin, barbital, benzocaine, benzoic acid, benzotropine, benzphetamine, berberine, bibucaine, bromazepan, brompheniramine, buprenorphine, buspirone, butabarbital, butacaine, butethal, caffeine, carbamazepine, carbromal, chloramphenicol, chlordiazepoxide, chloroquine, chlorothiazide, chloroxylenol, chlorphenesin, chlorpheniramine, chlorpromazine, chlorpropamide, chlortetracycline, cimetidine, cinchonidine, cinchonine, clenbuterol, clonazepam, clonixin, clorazepate, cocaine, codeine, colchicine, cortisone, coumarin, cyclazocine, cyclobenzaprine, cyclothiazide, cyheptamide, cymarin, danazol, danthron, dapsone, debrisoquine, desipramine, dexamethasone, dextromethorphan, dextropropoxyphene, diamorphine, diazepam, diclofenac, diethylpropion, diethylstilbestrol, diflunisal, digitoxin, digoxin, diltiazem, diphenhydramine, diphenoxylate, diprenorphine, dipyrone, disulfiram, dopamine, doxapram, doxepin, dronabinol, ephedrine, epinephrine, epinine, estradiol, estriol, estrone, ethacrynic acid, ethosuximide, etonitazene, etorphine, eugenol, famotidine, fenbendazole, fencamfamine, fenoprofen, fenproporex, fentanyl, flubendazole, flufenamic acid, flunitrazepam, 5-fluorouracil, fluoxymesterone, fluphenazine, furosemide, gentisic acid, gitoxigenin, glipizide, glunixin, glutethimide, glybenclamide, guaiacol, halazepam, haloperidol, hydrochlorothiazide, hydrocodone, hydrocortisone, hydromorphone, hydroxyquinoline, ibogaine, ibuprofen, iminostilbene, imipramine, indomethacin, isocarbostyril, isocarboxazid, isoniazid, isoproterenol, isoxsuprine, ivermectin, ketamine, ketoprofen, kynurenic acid, levorphanol, lidocaine, lorazepam, lormetazepam, loxapine, mazindol, mebendazole, meclizine, meclofenamic acid, medazepam, mefenamic acid, megestrol, mepacrine, meperidine, mephentermine, mephenytoin, mephesin, mephobarbital, mepivacaine, mescaline, mesoridazine, methadone, methamphetamine, methapyrilene, methaqualone, methazolamide, methocarbamol, methoxamine, methsuximide, methyl salicylate, methyldopa, methyldopamine, methylphenidate, methylprednisolone, methyltestosterone, methyprylon, metoprolol, mibolerone, morphine, nadolol, nalorphine, naloxone, naltrexone, naphazoline, naproxen, nefopam, niacinamide, nicotine, niacin, nifedipine, niflumic acid, nitrazepam, norepinephrine, nortriptyline, noscapine, nylidrin, oxazepam, oxycodone, oxymorphone, oxyphenbutazone, oxytetracycline, papaverine, pargyline, pemoline, pentazocine, pentobarbital, persantine, phenacetin, phenazocine, phenazopyridine, phencyclidine, phendimetrazine, phenelzine, pheniramine, phenobarbital, phenothiazine, phensuximide, phentermine, phenylbutazone, phenylephrine, phenylpropanolamine, piperocaine, prazepam, prednisolone, primidone, probenecid, progesterone, propiomazine, propranolol, propylparaben, pseudoephedrine, puromycin, pyrilamine, pyrithyldione, quazepam, quinaldic acid, quinidine, quinine, ranitidine, recinnamine, reserpine, resorcinol, saccharin, albuterol, salicylamide, salicylic acid, scopolamine, scopoletin, secobarbital, strychnine, sulfacetamide, sufadiazine, sulfadimethoxine, sulfaethidole, sulfamerazine, sulfamethazine, sulfamethoxizole, sulfanilamide, sulfapyridine, sulfasoxizole, sulindac, tamoxifen, temazepam, testosterone, tetracaine, tetracycline, tetramisole, thebaine, theobromine, theophylline, thiabendazole, thiamine, thiamylal, thiobarbituric acid, thioridazine, thiosalicylic acid, tolazamide, tolazoline, tobutamide, tolmetin, tranylcypromine, triamcinolone, tribenzylamine, trichloromethiazide, trifluoperazine, trihexyphenidyl, trimethoprim, tripelennamine, triprolidine, tropacocaine, tyramine, verapamil, vincamine, warfarin, yohimbine, zoxazolamine

REFERENCE

Hill,D.W.; Kind,A.J. Reversed-phase solvent gradient HPLC retention indexes of drugs, *J.Anal.Toxicol.*, **1994**, *18*, 233–242.

Thymopentin

Molecular formula: $C_{30}H_{49}N_9O_9$
Molecular weight: 679.77
CAS Registry No.: 69558-55-0
Merck Index: 9544



SAMPLE
Matrix: cell suspensions
Sample preparation: Centrifuge lymphocyte suspension for 10 s, inject an aliquot of the supernatant.

HPLC VARIABLES
Column: 300 × 3.9 10 μm C18 (Waters)
Mobile phase: MeCN:80 mM triethylammonium phosphate 4:96, pH 4.0 (Prepare buffer by adjusting 80 mM phosphoric acid to pH 4.0 with triethylamine.)
Flow rate: 1
Detector: UV 280

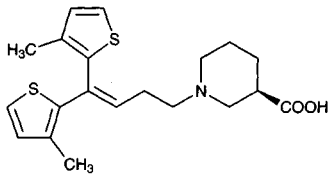
CHROMATOGRAM
Retention time: 7.5

OTHER SUBSTANCES
Simultaneous: degradation products

REFERENCE
Amoscato,A.A.; Balasubramaniam,A.; Alexander,J.W.; Babcock,G.F. Degradation of thymopentin by human lymphocytes: evidence for aminopeptidase activity, *Biochim.Biophys.Acta*, **1988**, *955*, 164–174.

Tiagabine

Molecular formula: $C_{20}H_{25}NO_2S_2$
Molecular weight: 375.56
CAS Registry No.: 115103-54-3
Merck Index: 9557



SAMPLE
Matrix: bulk
Sample preparation: Weigh out approximately 50 mg tiagabine, add 5 to 10 drops of MeOH, make up to 25 mL with isopropanol, inject an aliquot.

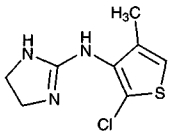
HPLC VARIABLES
Column: 250 × 4.6 Chiracel-OD (Daicel)
Mobile phase: EtOH:hexane:isopropanol:trifluoroacetic acid 6:80:14:0.5
Flow rate: 0.8
Injection volume: 10
Detector: UV 260

CHROMATOGRAM
Retention time: 10.1 (S(+)), 14.2 (R(-))

KEY WORDS
chiral

REFERENCE
Rustum,A.M.; Estrada,V. Separation and quantitation of the S-(+)-enantiomer in the bulk drug tiagabine.HCl by chiral high-performance-liquid chromatography using a Chiralcel-OD column, *J.Chromatogr.B*, **1998**, *705*, 111–117.

Tiamenidine



Molecular formula: $C_8H_{10}ClN_3S$
Molecular weight: 215.71
CAS Registry No.: 31428-61-2, 51274-83-0 (HCl)
Merck Index: 9558
Lednicer No.: 3 137

SAMPLE
Matrix: solutions

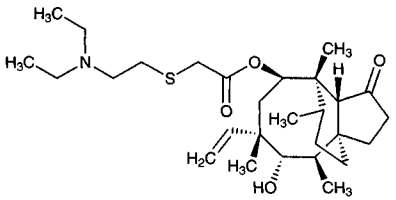
HPLC VARIABLES
Column: 150 × 4.6 12 μm 1-myristoyl-2-[(13-carboxyl)-tridecoyl]-sn-3-glycerophosphocholine chemically bonded to silica (Regis)
Mobile phase: MeCN:100 mM pH 7.0 phosphate buffer 20:80
Flow rate: 1
Detector: UV 254

CHROMATOGRAM
Retention time: k' 2.72

OTHER SUBSTANCES
Also analyzed: acebutolol, alprenolol, antazoline, atenolol, betaxolol, bisoprolol, bopindolol, bupranolol, carteolol, celiprolol, chloropyramine, chlorpheniramine, cicloprolol, cimetidine, cinnarizine, cirazoline, clonidine, dilevalol, dimethindene, diphenhydramine, doxazosin, esmolol, famotidine, isothipendyl, ketotifen, metiamide, metoprolol, moxonidine, nadolol, naphazoline, nifenalol, nizatidine, oxprenolol, pheniramine, phentolamine, pindolol, pizotyline (pizotifen), practolol, prazosin, promethazine, propranolol, pyrilamine (mepyramine), ranitidine, roxatidine, sotalol, timolol, tramazoline, tripelennamine, triprolidine, tymazoline, UK-14,304

REFERENCE
Kaliszan,R.; Nasal,A.; Turowski,M. Binding site for basic drugs on α_1-acid glycoprotein as revealed by chemometric analysis of biochromatographic data, *Biomed.Chromatogr.*, **1995**, *9*, 211–215.

Tiamulin



Molecular formula: $C_{28}H_{47}NO_4S$
Molecular weight: 493.75
CAS Registry No.: 55297-95-5, 55297-96-6 (fumarate)
Merck Index: 9559

SAMPLE
Matrix: feed
Sample preparation: 50 g Milled feed + 250 mL 1% sodium carbonate + 250 mL hexane:ethyl acetate 75:25, homogenize (Silverson) for 1 min, centrifuge at 2000 rpm for 5 min. Remove a 10 mL aliquot of the upper solvent layer and add it to 10 mL 0.1% tartaric acid, rotate for 1 min, centrifuge at 2000 rpm for 5 min, inject a 0.4-3 mL aliquot of the aqueous layer.

HPLC VARIABLES
Column: 200 × 4.6 5 μm Hypersil-ODS
Mobile phase: MeCN:MeOH:1% ammonium carbonate 30:60:20
Flow rate: 1.5
Injection volume: 400-3000
Detector: UV 250

CHROMATOGRAM
Retention time: 12
Limit of detection: <5 μg/g

OTHER SUBSTANCES
Noninterfering: furazolidone, monensin, sulfadimidine

REFERENCE
Howard,D.; Cowen,T. Determination of tiamulin hydrogen fumarate in animal feeds using high-performance liquid chromatography, *Analyst*, **1982**, *107*, 319–323.

SAMPLE
Matrix: feed, formulations, premix
Sample preparation: Premix. 5 g Premix + 250 mL 1% sodium carbonate, shake for 30 min, add 250 mL hexane:ethyl acetate 75:25, shake for 1 h, shake vigorously by hand for 15-20 s, let stand until layers separate (centrifuge if necessary). Remove a 10 mL aliquot of the upper organic layer and add it to 30 mL 0.1% tartaric acid, shake gently horizontally for 30 s, inject a 50 μL aliquot of the lower aqueous layer. Formulations. Weigh out 660 mg formulation, add 100 mL water, shake or sonicate for 1 h, filter (44 μm) an aliquot, inject an aliquot of the filtrate (J. AOAC Int. 1993, 76, 447). Feed. 50 g Feed + 250 mL hexane:ethyl acetate 75:25 + 250 mL 1% sodium carbonate, shake in an orbital shaker at 250 rpm for 1 h, let stand for 1 h, centrifuge the supernatant at 1500 rpm for 15 min. Remove a 75 mL aliquot of the upper organic layer and add it to 5 mL 0.1% tartaric acid, shake gently horizontally for 30 s, repeat extraction twice more, combine the aqueous layers, inject a 50 μL aliquot of the lower aqueous layer (J. AOAC Int. 1993, 76, 449).

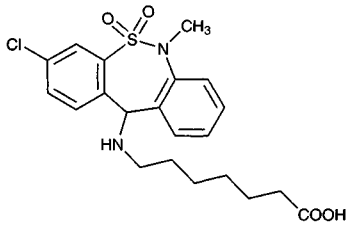
HPLC VARIABLES
Guard column: CO:PELL ODS
Column: 250 × 4.6 5 μm Hypersil ODS (premix, feed) or 300 × 3.9 10 μm C18 (formulations)
Mobile phase: MeCN:MeOH:1% ammonium carbonate 30:60:25 (Pass mobile phase through a column of 200-425 mesh Adsorbosil silica (Alltech) before injector. Periodically wash column with 60 mL MeOH:1% acetic acid and 30 mL MeOH, then re-equilibrate with mobile phase.)
Flow rate: 1.5
Injection volume: 50
Detector: UV 254

CHROMATOGRAM
Retention time: 7

KEY WORDS
powders

REFERENCE
Markus,J.R.; Sherma,J. Method. I. Liquid chromatographic determination of tiamulin hydrogen fumarate in feed premixes, *J.AOAC Int.*, **1993**, *76*, 444–446.

Tianeptine



Molecular formula: $C_{21}H_{25}ClN_2O_4S$
Molecular weight: 436.96
CAS Registry No.: 66981-73-5
Merck Index: 9560

SAMPLE

Matrix: blood

Sample preparation: 2 mL Whole blood or plasma + 2 mL buffer + 5 mL chloroform:isopropanol: n-heptane 60:14:26, shake gently horizontally for 10 min, centrifuge at 2800 g for 10 min. Remove the lower organic layer and evaporate it to dryness under vacuum at 45°, reconstitute the residue in 100 μL mobile phase, centrifuge at 2800 g for 5 min, inject a 50 μL aliquot of the supernatant. (Buffer was saturated ammonium chloride solution 25% diluted with water, adjusted to pH 9.5 with 25% ammonia solution.)

HPLC VARIABLES

Column: 300 × 3.9 4 μm NovaPack C18

Mobile phase: MeOH:THF:buffer 65:5:30 (Buffer was 0.68 g/L (10 mM (sic)) KH_2PO_4 adjusted to pH 2.6 with concentrated orthophosphoric acid.) (At the end of each session wash the column with water for 1 h and MeOH for 1 h, re-equilibrate for 30 min.)

Column temperature: 30

Flow rate: 0.8

Injection volume: 50

Detector: UV 269

CHROMATOGRAM

Retention time: 5.40

Limit of detection: <120 ng/mL

KEY WORDS

whole blood; plasma; interferences may occur–compounds (all of which are extracted) elute in this order tenoxicam; iproniazid; methocarbamol; methotrexate; caffeine; nialamide; colchicine; cytarabine; benzoylecgonine; acetaminophen; diazoxide; dacarbazine; sulfinpyrazole; flumazenil; sulpride; morphine; atenolol; toloxatone; terbutaline; albuterol; phenobarbital; ranitidine; tiapride; phenol; chlormezanone; aspirin; metformin; ritodrine; codeine; sultopride; amisulpride; naltrexone; lisinopril; benzocaine; nizatidine; nalorphine; mephenesin; naloxone; sotalol; carteolol; procainamide; carbamazepine; bromazepam; nalbuphine; nadolol; procarbazine; dihydralazine; omeprazole; strychnine; acebutolol; glutethimide; chlorpropamide; glipizide; triazolam; prazosin; flunitrazepam; clonazepam; metoclopramide; melphalan; estazolam; tolbutamide; ephedrine; clonidine; pindolol; clobazam; minoxidil; disopyramide; nitrazepam; dextromethorphan; tofisopam; zopiclone; debrisoquine; sulindac; alprazolam; cycloguanil; lorazepam; methaqualone; ketamine; piroxicam; metoprolol; nifedipine; quinine; mephentermine; prilocaine; pentazocine; oxazepam; tiaprofenic acid; quinidine; celiprolol; ajmaline; yohimbine; lidocaine; secobarbital; viloxazine; mepivacaine; meperidine; doxylamine; labetalol; temazepam; amodiaquine; benperidol; droperidol; hydroxychloroquine; zolpidem; ketoprofen; alminoprofen; cicletanine; moclobemide; chloroquine; cocaine; timolol; nomifensine; ticlopidine; acenocoumarol; vindesine; mexiletine; dipyridamole; trazodone; pipamperone; pyrimethamine; benazepril; vincristine; metapramine; chlordiazepoxide; oxprenolol; warfarin; clorazepate; flecainide; phencyclidine; thiopental; fenfluramine; metipranolol; triprolidine; naproxen; buprenorphine; verapamil; buspirone; tianeptine; midazolam; bupivacaine; carbinoxamine; loprazolam; cetirizine; chlorpheniramine; moperone; cibenzoline; medifoxamine; astemizole; vinblastine; nicardipine; bisoprolol; diltiazem; glibornuride; reserpine; aconitine; nitrendipine; diazepam; mianserin; ramipril; haloperidol; tetracaine; alprenolol; acepromethazine; glibenclamide; chlorophenacinone; doxepin; nimodipine; diphenhydramine; cyclizine; histapyrrodine; phenylbutazone; demexiptiline; clozapine; proguanil; trifluperidol; medazepam; cyamemazine; bumadizone; suriclone; propranolol; acepromazine; dothiepin; dextromoramide; fenoprofen; dextropropoxyphene; loxapine; betaxolol; propafenone; promethazine; thioproperazine; methadone; amoxapine; quinupramine; opipramol; cyproheptadine; brompheniramine; mefenidra-

mine; protriptyline; flurbiprofen; tetrazepam; zorubicin; prazepam; alimemazine; loperamide; imipramine; desipramine; levomepromazine; hydroxyzine; niflumic acid; penbutolol; fluvoxamine; pimozide; daunorubicin; indomethacin; maprotiline; tropatenine; etodolac; fluoxetine; amitriptyline; nortriptyline; tioclomarol; diclofenac; mefloquine; trimipramine; chlorambucil; lidoflazine; ibuprofen; floctafenine; alpidem; loratadine; chlorpromazine; clomipramine; carpipramine; thioridazine; fentiazac; clemastine; mefenamic acid; fluphenazine; prochlorperazine; penfluridol; bepridil; terfenadine; trifluoperazine

REFERENCE

Tracqui,A.; Kintz,P.; Mangin,P. Systematic toxicological analysis using HPLC/DAD, *J.Forensic Sci.*, **1995**, *40*, 254–262.

SAMPLE

Matrix: blood, tissue, urine

Sample preparation: Plasma, urine. Centrifuge urine at 900 g. 2 mL Plasma or centrifuged urine + 1 mL 50 (plasma) or 500 (urine) mM pH 7.0 phosphate buffer + 100 μL 10 μg/mL IS in water + 10 mL heptane:octanol 98:2 containing 5 g/L tetraheptylammonium bromide, shake for 10 min, centrifuge at 900 g for 10 min. Remove an 8 mL aliquot of the upper aqueous phase and add it to 200 μL MeOH:170 mM acetic acid 10:90, shake on a rotary agitator at 10 rpm for 5 min, centrifuge at 900 g for 5 min, inject a 50 μL aliquot of the aqueous phase. Brain. Homogenize (Ultra Turrax) 1 g brain tissue and 2 mL 50 mM pH 7.0 phosphate buffer for 30 s, vortex for 15 s, centrifuge. 2 mL Supernatant + 1 mL 50 mM pH 7.0 phosphate buffer + 100 μL 10 μg/mL IS in water + 10 mL heptane:octanol 98:2 containing 5 g/L tetraheptylammonium bromide, shake for 10 min, centrifuge at 900 g for 10 min. Remove an 8 mL aliquot of the upper aqueous phase and add it to 200 μL MeOH:170 mM acetic acid 10:90, shake on a rotary agitator at 10 rpm for 5 min, centrifuge at 900 g for 5 min, inject a 50 μL aliquot of the aqueous phase.

HPLC VARIABLES

Column: 150 × 4.6 5 μm Hypersil ODS

Mobile phase: MeCN:buffer 45:55 (Buffer was 2.7 g/L sodium pentanesulfonate adjusted to pH 3.0 with phosphoric acid.)

Flow rate: 1.3

Injection volume: 50

Detector: UV 220

CHROMATOGRAM

Retention time: 4.5

Internal standard: (dihydro-10,11-dibenzo[a,d]cycloheptenyl-5-amino)-7-octanoic acid (Servier Labs) (6.0)

Limit of detection: 10 ng/mL

OTHER SUBSTANCES

Extracted: metabolites

Simultaneous: bromazepam, clobazam, clonazepam, clorazepate, desmethyldiazepam, flunitrazepam, lorazepam, nitrazepam, oxazepam, triazolam

Noninterfering: clomipramine, desipramine, desmethylclomipramine, imipramine, medazepam, meprobamate, nortriptyline, protriptyline, tetrazepam, trimipramine

Interfering: amineptine, diazepam

KEY WORDS

plasma; human; rat; brain; pharmacokinetics

REFERENCE

Nicot,G.; Lachatre,G.; Gonnet,C.; Mallon,J.; Mocaer,E. Ion-pair extraction and high-performance liquid chromatographic determination of tianeptine and its metabolites in human plasma, urine and tissues, *J.Chromatogr.*, **1986**, *381*, 115–126.

SAMPLE

Matrix: blood, urine

Sample preparation: Add 1 mL whole blood or urine to Toxi-Tube A (Toxi-Lab, Irvine CA), add 3 mL water, mix by gentle inversion for 5 min, centrifuge at 1500 g for 5 min. Remove the

organic layer and evaporate it to dryness under a stream of nitrogen at 40°, reconstitute the residue with 50 μL MeCN:water 50:50, vortex for 10 s, centrifuge at 7500 g for 2 min, inject a 10 (urine) or 30 (blood) μL aliquot. (The detector wavelength shown is the wavelength of maximum absorbance. This will not necessarily be the optimal wavelength for the separation. Multiple wavelengths from 200-350 nm can be scanned using a diode-array detector. Otherwise, 220 nm may be a reasonable choice for initial work. Matrix may interfere.)

HPLC VARIABLES
Guard column: 20 mm long Symmetry C18
Column: 250 × 4.6 5 μm Symmetry C8 (Waters)
Mobile phase: Gradient. A was 50 mM pH 3.8 sodium phosphate buffer. B was MeCN. A:B 85:15 for 6.5 min, 65:35 for 18.5 min, 20:80 for 3 min (step gradient), re-equilibrate at initial conditions for 7 min.
Column temperature: 30
Flow rate: 1 for 6.5 min, to 1.5 over 18.5 min, maintain at 1.5 for 3 min (re-equilibrate at 1.5 mL/min)
Injection volume: 10-30
Detector: UV 206.4

CHROMATOGRAM
Retention time: 14.877

KEY WORDS
whole blood

REFERENCE
Gaillard,Y.; Pépin,G. Use of high-performance liquid chromatography with photodiode-array UV detection for the creation of a 600-compound library. Application to forensic toxicology, *J.Chromatogr.A*, **1997**, *763*, 149–163.

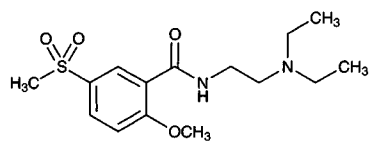
SAMPLE
Matrix: urine
Sample preparation: Inject directly.

HPLC VARIABLES
Column: 125 × 4.8 10 μm Lichrosorb RP 18
Mobile phase: Gradient. MeCN:10 mM pH 5.5 phosphate buffer from 0:100 to 100:0 over 105 min.
Flow rate: 1
Injection volume: 72
Detector: radioactivity

OTHER SUBSTANCES
Extracted: metabolites

REFERENCE
Grislain,L.; Gele,P.; Bertrand,M.; Luijten,W.; Bromet,N.; Salvadori,C.; Kamoun,A. The metabolic pathways of tianeptine, a new antidepressant, in healthy volunteers, *Drug Metab.Dispos.*, **1990**, *18*, 804–808.

Tiapride



Molecular formula: $C_{15}H_{24}N_2O_4S$
Molecular weight: 328.43
CAS Registry No.: 51012-32-9, 51012-33-0 (HCl)
Merck Index: 9561

SAMPLE
Matrix: blood

Sample preparation: Mix 1 mL plasma with 4 mL 500 mM NaOH and 2 g NaCl. Add 10 mL MTBE, shake for 10 min and centrifuge at 850 g for 10 min. Remove the solvent layer, mix with 2.5 mL 100 mM HCl, shake for 10 min and centrifuge at 850 g for 10 min. Remove the aqueous layer, add it to 1 mL 500 mM NaOH, 1.5 g NaCl and 2 mL MTBE, shake for 10 min and centrifuge. Remove the solvent layer and evaporate to dryness under a stream of nitrogen. Reconstitute the residue in 50 μL MeCN and inject a 10 μL aliquot.

HPLC VARIABLES
Column: 150 × 2.1 I.D. 5 μm Hypersil
Mobile phase: MeCN:100 mM ammonium acetate 94:6
Column temperature: 40
Flow rate: 0.4
Injection volume: 10
Detector: UV 240; MS, Hewlett-Packard Model 59980A, particle beam nebulizer helium 35 psi, solvation chamber 60°, Model 5989A, NICI mode, reagent gas methane at 1 torr, source 250°, negative ion chemical ionization mode, reagent gas methane at 1 torr, source 250 .deg., m/z 313.

CHROMATOGRAM
Retention time: 11.0
Internal standard: tiapride

OTHER SUBSTANCES
Extracted: sultopride

KEY WORDS
plasma; tiapride is IS

REFERENCE
Jitsufuchi,N.; Kudo,K.; Tokunaga,H.; Imamura,T. Selective determination of sultopride in human plasma using high-performance liquid chromatography with ultraviolet detection and particle beam mass spectrometry, *J.Chromatogr.B*, **1997**, *690*, 153–159.

SAMPLE
Matrix: blood, urine
Sample preparation: Add 1 mL whole blood or urine to Toxi-Tube A (Toxi-Lab, Irvine CA), add 3 mL water, mix by gentle inversion for 5 min, centrifuge at 1500 g for 5 min. Remove the organic layer and evaporate it to dryness under a stream of nitrogen at 40°, reconstitute the residue with 50 μL MeCN:water 50:50, vortex for 10 s, centrifuge at 7500 g for 2 min, inject a 10 (urine) or 30 (blood) μL aliquot. (The detector wavelength shown is the wavelength of maximum absorbance. This will not necessarily be the optimal wavelength for the separation. Multiple wavelengths from 200-350 nm can be scanned using a diode-array detector. Otherwise, 220 nm may be a reasonable choice for initial work. Matrix may interfere.)

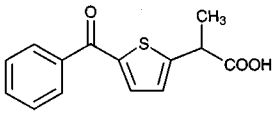
HPLC VARIABLES
Guard column: 20 mm long Symmetry C18
Column: 250 × 4.6 5 μm Symmetry C8 (Waters)
Mobile phase: Gradient. A was 50 mM pH 3.8 sodium phosphate buffer. B was MeCN. A:B 85:15 for 6.5 min, 65:35 for 18.5 min, 20:80 for 3 min (step gradient), re-equilibrate at initial conditions for 7 min.
Column temperature: 30
Flow rate: 1 for 6.5 min, to 1.5 over 18.5 min, maintain at 1.5 for 3 min (re-equilibrate at 1.5 mL/min)
Injection volume: 10-30
Detector: UV 213.4

CHROMATOGRAM
Retention time: 5.468

KEY WORDS
whole blood

REFERENCE
Gaillard,Y.; Pépin,G. Use of high-performance liquid chromatography with photodiode-array UV detection for the creation of a 600-compound library. Application to forensic toxicology, *J.Chromatogr.A*, **1997**, *763*, 149–163.

Tiaprofenic acid



Molecular formula: $C_{14}H_{12}O_3S$
Molecular weight: 260.31
CAS Registry No.: 33005-95-7
Merck Index: 9562

SAMPLE
Matrix: blood
Sample preparation: 2 mL Whole blood or plasma + 2 mL buffer + 5 mL chloroform:isopropanol: n-heptane 60:14:26, shake gently horizontally for 10 min, centrifuge at 2800 g for 10 min. Remove the lower organic layer and evaporate it to dryness under vacuum at 45°, reconstitute the residue in 100 μL mobile phase, centrifuge at 2800 g for 5 min, inject a 50 μL aliquot of the supernatant. (Buffer was saturated ammonium chloride solution 25% diluted with water, adjusted to pH 9.5 with 25% ammonia solution.)

HPLC VARIABLES
Column: 300 × 3.9 4 μm NovaPack C18
Mobile phase: MeOH:THF:buffer 65:5:30 (Buffer was 0.68 g/L (10 mM (sic)) KH_2PO_4 adjusted to pH 2.6 with concentrated orthophosphoric acid.) (At the end of each session wash the column with water for 1 h and MeOH for 1 h, re-equilibrate for 30 min.)
Column temperature: 30
Flow rate: 0.8
Injection volume: 50
Detector: UV 307

CHROMATOGRAM
Retention time: 4.34
Limit of detection: <120 ng/mL

KEY WORDS
whole blood; plasma; interferences may occur–compounds (all of which are extracted) elute in this order tenoxicam; iproniazid; methocarbamol; methotrexate; caffeine; nialamide; colchicine; cytarabine; benzoylecgonine; acetaminophen; diazoxide; dacarbazine; sulfinpyrazole; flumazenil; sulpride; morphine; atenolol; toloxatone; terbutaline; albuterol; phenobarbital; ranitidine; tiapride; phenol; chlormezanone; aspirin; metformin; ritodrine; codeine; sultopride; amisulpride; naltrexone; lisinopril; benzocaine; nizatidine; nalorphine; mephenesin; naloxone; sotalol; carteolol; procainamide; carbamazepine; bromazepam; nalbuphine; nadolol; procarbazine; dihydralazine; omeprazole; strychnine; acebutolol; glutethimide; chlorpropamide; glipizide; triazolam; prazosin; flunitrazepam; clonazepam; metoclopramide; melphalan; estazolam; tolbutamide; ephedrine; clonidine; pindolol; clobazam; minoxidil; disopyramide; nitrazepam; dextromethorphan; tofisopam; zopiclone; debrisoquine; sulindac; alprazolam; cycloguanil; lorazepam; methaqualone; ketamine; piroxicam; metoprolol; nifedipine; quinine; mephentermine; prilocaine; pentazocine; oxazepam; tiaprofenic acid; quinidine; celiprolol; ajmaline; yohimbine; lidocaine; secobarbital; viloxazine; mepivacaine; meperidine; doxylamine; labetalol; temazepam; amodiaquine; benperidol; droperidol; hydroxychloroquine; zolpidem; ketoprofen; alminoprofen; cicletanine; moclobemide; chloroquine; cocaine; timolol; nomifensine; ticlopidine; acenocoumarol; vindesine; mexiletine; dipyridamole; trazodone; pipamperone; pyrimethamine; benazepril; vincristine; metapramine; chlordiazepoxide; oxprenolol; warfarin; clorazepate; flecainide; phencyclidine; thiopental; fenfluramine; metipranolol; triprolidine; naproxen; buprenorphine; verapamil; buspirone; tianeptine; midazolam; bupivacaine; carbinoxamine; loprazolam; cetirizine; chlorpheniramine; moperone; cibenzoline; medifoxamine; astemizole; vinblastine; nicardipine; bisoprolol; diltiazem; glibornuride; reserpine; aconitine; nitrendipine; diazepam; mianserin; ramipril; haloperidol; tetracaine; alprenolol; acepromazine; glibenclam-

ide; chlorophenacinone; doxepin; nimodipine; diphenhydramine; cyclizine; histapyrrodine; phenylbutazone; demexiptiline; clozapine; proguanil; trifluperidol; medazepam; cyamemazine; bumadizone; suriclone; propranolol; acepromazine; dothiepin; dextromoramide; fenoprofen; dextropropoxyphene; loxapine; betaxolol; propafenone; promethazine; thioproperazine; methadone; amoxapine; quinupramine; opipramol; cyproheptadine; brompheniramine; mefenidramine; protriptyline; flurbiprofen; tetrazepam; zorubicin; prazepam; alimemazine; loperamide; imipramine; desipramine; levomepromazine; hydroxyzine; niflumic acid; penbutolol; fluvoxamine; pimozide; daunorubicin; indomethacin; maprotiline; tropatenine; etodolac; fluoxetine; amitriptyline; nortriptyline; tioclomarol; diclofenac; mefloquine; trimipramine; chlorambucil; lidoflazine; ibuprofen; floctafenine; alpidem; loratadine; chlorpromazine; clomipramine; carpipramine; thioridazine; fentiazac; clemastine; mefenamic acid; fluphenazine; prochlorperazine; penfluridol; bepridil; terfenadine; trifluoperazine

REFERENCE

Tracqui,A.; Kintz,P.; Mangin,P. Systematic toxicological analysis using HPLC/DAD, *J.Forensic Sci.*, **1995**, *40*, 254–262.

SAMPLE

Matrix: blood

Sample preparation: 500 μL Plasma + 50 μL 100 μg/mL ketorolac + 100 μL 600 mM sulfuric acid + 3 mL isooctane:isopropanol 95:5, vortex for 30 s, centrifuge at 1800 g for 5 min. Remove the organic layer and evaporate it to dryness, reconstitute the residue in 100 μL 2 mg/mL 4-(dimethylamino)pyridine in MeCN, add 100 μL 60 mM trichloroethyl chloroformate in MeCN, add 1 M L-leucinamide in MeCN, let stand for 2 min, add 500 μL 250 mM HCl, extract with chloroform. Remove the organic layer and evaporate it to dryness, reconstitute the residue in mobile phase, inject a 10-100 μL aliquot. (A 7% conversion of S to R is observed during the derivatization procedure. No racemization is observed using a direct procedure with a chiral column.)

HPLC VARIABLES

Column: 100 × 4.6 5 μm Partisil 5 ODS-2
Mobile phase: MeCN:60 mM KH_2PO_4:triethylamine 30:70:0.02
Flow rate: 1
Injection volume: 10-100
Detector: UV 310

CHROMATOGRAM

Retention time: 17.2 (R), 19.5 (S)
Internal standard: ketorolac (10.7 (R), 19.5 (S))
Limit of quantitation: 50 ng/mL

KEY WORDS

derivatization; chiral; plasma; comparison with a method involving a chiral column; pharmacokinetics

REFERENCE

Vakily,M.; Jamali,F. Pharmacokinetics of tiaprofenic acid in humans: Lack of stereoselectivity in plasma using both direct and precolumn derivatization methods, *J.Pharm.Sci.*, **1996**, *85*, 638–642.

SAMPLE

Matrix: blood, urine

Sample preparation: Plasma. 2 mL Plasma + 50 μL 50 μg/mL IS in MeOH + 250 μL 1 M HCl + 5 mL diethyl ether, mix, centrifuge at 1100 g for 10 min. Remove the organic phase, repeat the extraction, combine the organic extracts, evaporate under nitrogen at 40°, reconstitute the residue in 200 μL mobile phase, vortex, inject a 20 μL aliquot. Urine. 1 mL Urine + 250 μL 1 M HCl + 50 μL IS + 5 mL diethyl ether, rotate for 15 min. Remove the organic layer, add 1 mL 1% sodium hydrogen carbonate, vortex for 1 min. Remove the organic layer and evaporate it under nitrogen at 40°, reconstitute the residue in 200 μL mobile phase, inject a 20 μL aliquot.

HPLC VARIABLES

Column: 100 × 3 5 μm Nucleosil
Mobile phase: MeCN:water:acetic acid 40:59.4:0.6

Column temperature: 35
Flow rate: 0.8
Injection volume: 20
Detector: UV 310

CHROMATOGRAM
Retention time: 2.7
Internal standard: feprazone (8.3, UV 245))
Limit of quantitation: 100 ng/mL (plasma), 500 ng/mL (urine)

OTHER SUBSTANCES
Noninterfering: alclofenac, diclofenac, fenoprofen, flunixin, flurbiprofen, ibuprofen, indomethacin, naproxen, oxyphenbutazone, phenylbytazone, piroxicam

KEY WORDS
plasma; pharmacokinetics

REFERENCE
Delbeke,F.T.; Baert,K.; De Backer,P. Disposition of human drug preparations in the horse. VI. Tiaprofenic acid, *J.Chromatogr.B*, **1997**, *704*, 207–214.

SAMPLE
Matrix: blood, urine
Sample preparation: Add 1 mL whole blood or urine to Toxi-Tube A (Toxi-Lab, Irvine CA), add 3 mL water, mix by gentle inversion for 5 min, centrifuge at 1500 g for 5 min. Remove the organic layer and evaporate it to dryness under a stream of nitrogen at 40°, reconstitute the residue with 50 μL MeCN:water 50:50, vortex for 10 s, centrifuge at 7500 g for 2 min, inject a 10 (urine) or 30 (blood) μL aliquot. (The detector wavelength shown is the wavelength of maximum absorbance. This will not necessarily be the optimal wavelength for the separation. Multiple wavelengths from 200-350 nm can be scanned using a diode-array detector. Otherwise, 220 nm may be a reasonable choice for initial work. Matrix may interfere.)

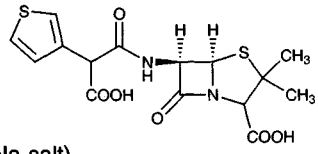
HPLC VARIABLES
Guard column: 20 mm long Symmetry C18
Column: 250 × 4.6 5 μm Symmetry C8 (Waters)
Mobile phase: Gradient. A was 50 mM pH 3.8 sodium phosphate buffer. B was MeCN. A:B 85:15 for 6.5 min, 65:35 for 18.5 min, 20:80 for 3 min (step gradient), re-equilibrate at initial conditions for 7 min.
Column temperature: 30
Flow rate: 1 for 6.5 min, to 1.5 over 18.5 min, maintain at 1.5 for 3 min (re-equilibrate at 1.5 mL/min)
Injection volume: 10-30
Detector: UV 200.5

CHROMATOGRAM
Retention time: 17.653

KEY WORDS
whole blood

REFERENCE
Gaillard,Y.; Pépin,G. Use of high-performance liquid chromatography with photodiode-array UV detection for the creation of a 600-compound library. Application to forensic toxicology, *J.Chromatogr.A*, **1997**, *763*, 149–163.

Ticarcillin



Molecular formula: $C_{15}H_{16}N_2O_6S_2$
Molecular weight: 384.43
CAS Registry No.: 34787-01-4, 4697-14-7 (di Na salt), 74682-62-5 (Na salt)
Merck Index: 9568
Lednicer No.: 2 437

SAMPLE

Matrix: bile, blood, urine
Sample preparation: Serum. 0.5 mL serum + 0.5 mL MeCN mix in 7 mL tube on vortex mixer; shake by rotation (20 rpm) 10 min; centrifuge 10 min 1000 g; transfer supernatant to another tube, add 7 aliquots dichloromethane; equilibrate 10 min; shake by rotation (20 rpm) 10 min; centrifuge 10 min 1000 g; inject aliquot of upper aqueous layer. Urine. Centrifuge urine and dilute 1:20. Bile. Centrifuge bile and dilute 1:10

HPLC VARIABLES

Column: 75 × 4.6 3 μm octadecylsilane
Mobile phase: 36:64 MeCN:10 mM citrate buffer adjusted to pH 2 with HCl
Flow rate: 1
Injection volume: 5
Detector: UV 214

CHROMATOGRAM

Retention time: 1.6
Limit of detection: 100 ng/mL

OTHER SUBSTANCES

Also analyzed: ampicillin, azlocillin, aztreonam, cefmenoxime, cefoperazone, cefsulodin, cefotaxime, ceftazidime, ceftriaxone, cloxacillin, desacetylcefotaxime, mezlocillin, penicillin G, piperacillin

KEY WORDS

serum

REFERENCE

Jehl,F.; Birckel,P.; Monteil,H. Hospital routine analysis of penicillins, third-generation cephalosporins and aztreonam by conventional and high-speed high-performance liquid chromatography, *J.Chromatogr.*, **1987**, *413*, 109–119.

SAMPLE

Matrix: blood
Sample preparation: 350 μL Serum + 150 μL 150 μg/mL temocillin in water + 250 μL 400 mM HCl + 3.5 mL chloroform:n-amyl alcohol (3:1), mix for 5 min, centrifuge for 5 min. Remove the organic layer and add it to 350 μL 10 mM pH 7.0 phosphate buffer, mix for 5 min, centrifuge for 5 min, inject a 20 μL aliquot of the upper aqueous layer.

HPLC VARIABLES

Column: 300 × 3.9 10 μm μBondapak C18
Mobile phase: MeOH:buffer 15:85 (Buffer was 100 mM ammonium acetate adjusted to pH 4.0 with glacial acetic acid.)
Flow rate: 1.8
Injection volume: 20
Detector: UV 242

CHROMATOGRAM

Retention time: 6.8
Internal standard: temocillin (5.4)

OTHER SUBSTANCES
Simultaneous: cefoxitin
Noninterfering: acetaminophen, acetazolamide, allopurinol, amikacin, ampicillin, azlocillin, caffeine, cefamandole, cefoperazone, cefotaxime, cefsulodin, ceftazidime, ceftizoxime, chloramphenicol, chlorpromazine, clindamycin, dicloxacillin, 5-fluorocytosine, flurazepam, gentamicin, methicillin, metronidazole, mezlocillin, moxalactam, nafcillin, penicillin, phenobarbital, piperacillin, procainamide, rifampin, sulfamethoxazole, theophylline, thienamycin, tobramycin, trimethoprim, vancomycin
Interfering: cefuroxime, cephalothin

KEY WORDS
serum

REFERENCE
Shull,V.H.; Dick,J.D. Determination of ticarcillin levels in serum by high-pressure liquid chromatography, *Antimicrob.Agents Chemother.*, **1985**, *28*, 597–600.

SAMPLE
Matrix: blood, urine
Sample preparation: Serum. 200 μL Serum + 200 μL 10 M urea, mix, filter (Amicon MPS-1 micropartition system with Amicon YMT membranes) while centrifuging at 1500 g for 10 min. Add 200 μL of the ultrafiltrate to 200 μL reagent and heat at 60° for 10 min, cool to room temperature, inject a 30-90 μL aliquot. Urine. Dilute urine 10-fold with water, filter (0.45 μm acrylate copolymer). Add 200 μL of the filtrate to 200 μL reagent and heat at 60° for 10 min, cool to room temperature, inject a 30-60 μL aliquot. (Prepare reagent by dissolving 13.81 g 1,2,4-triazole in 60 mL water, add 10 mL 2.7 mg/mL mercury(II) chloride in water, adjust pH to 9.0 ± 0.05 with saturated NaOH, make up to 100 mL with water.)

HPLC VARIABLES
Column: 150 × 4.6 5 μm Develosil ODS-5 (Nomura Chemicals)
Mobile phase: MeCN:buffer containing 5 mM tetrabutylammonium bromide and 5 mM sodium thiosulfate 1:1.8 (Prepare the buffer by dissolving 14.32 g $Na_2HPO_4.12H_2O$ and 6.240 g $NaH_2PO_4.2H_2O$ in 1 L water then diluting 100-fold.)
Column temperature: 40
Flow rate: 1
Injection volume: 30-90
Detector: UV 328

CHROMATOGRAM
Retention time: 4.5
Limit of detection: 1 μg/mL (urine), 100 ng/mL (plasma)

OTHER SUBSTANCES
Interfering: carbenicillin

KEY WORDS
serum; derivatization; ultrafiltrate; pharmacokinetics

REFERENCE
Haginaka,J.; Wakai,J. High-performance liquid chromatographic assay of carbenicillin, ticarcillin and sulbenicillin in serum and urine using pre-column reaction with 1,2,4-triazole and mercury(II) chloride, *Analyst*, **1985**, *110*, 1185–1188.

SAMPLE
Matrix: blood, urine
Sample preparation: Plasma. 200 μL Plasma + 500 μL 2 μg/mL cefoperazone in MeCN, vortex for 20 s, centrifuge at 3000 rpm for 10 min. Remove the organic layer and evaporate it to dryness under a stream of nitrogen, reconstitute the residue in 200 μL mobile phase, inject a 10-15 μL aliquot. Urine. Inject a 102-20 μL aliquot directly onto the column.

HPLC VARIABLES
Column: 250 × 4.6 5 μm Adsorbosphere C18

Mobile phase: MeCN:water:orthophosphoric acid:10% tetramethylammonium chloride 30:69.6:0.1:0.3
Flow rate: 1
Injection volume: 10-20
Detector: UV 205

CHROMATOGRAM
Retention time: 8.8
Internal standard: cefoperazone (6.8)
Limit of detection: 1000 ng/mL (urine), 500 ng/mL (plasma)

OTHER SUBSTANCES
Noninterfering: xanthines, aspirin, acetaminophen, cephalosporins, penicillins

KEY WORDS
plasma; pharmacokinetics

REFERENCE
La Follette,G.; Jayewardene,A.L.; Seneviratne,A.K.; Lin,E.T.; Gambertoglio,J.G. Determination of ticarcillin in human plasma by reversed-phase LC, *J.Pharm.Biomed.Anal.*, **1995**, *13*, 159–164.

SAMPLE
Matrix: bulk
Sample preparation: Prepare a 300 μg/mL solution in 100 mM pH 7.0 phosphate buffer, inject a 20 μL aliquot.

HPLC VARIABLES
Column: 300 × 3.9 μBondapak C18
Mobile phase: MeOH:buffer 10:90 (Buffer was 15.6 g $NaH_2PO_4.2H_2O$ in 900 mL water, adjust pH to 7.0 with NaOH, make up to 1 L with water.)
Flow rate: 2
Injection volume: 20
Detector: UV 230

CHROMATOGRAM
Retention time: 10.5 (R), 12.0 (S)

OTHER SUBSTANCES
Simultaneous: isomers, temocillin

REFERENCE
Bird,A.E.; Charsley,C.H.; Jennings,K.R.; Marshall,A.C. High-performance liquid chromatographic assay of temocillin and epimerisation of its diastereoisomers, *Analyst*, **1984**, *109*, 1209–1212.

SAMPLE
Matrix: formulations
Sample preparation: Dilute with water (if necessary), inject a 20 μL aliquot.

HPLC VARIABLES
Column: 300 × 4 μBondapak phenyl
Mobile phase: 10 mM ammonium acetate
Flow rate: 1.6
Injection volume: 20
Detector: UV 245

CHROMATOGRAM
Retention time: 4.5, 5 (two isomers)

OTHER SUBSTANCES
Interfering: carbenicillin

KEY WORDS
saline; 5% dextrose; stability-indicating

REFERENCE
Das Gupta,V.; Stewart,K.R. Quantitation of carbenicillin disodium, cefazolin sodium, cephalothin sodium, nafcillin sodium, and ticarcillin disodium by high-pressure liquid chromatography, *J.Pharm.Sci.*, **1980**, *69*, 1264–1267.

SAMPLE
Matrix: formulations
Sample preparation: Dilute with mobile phase, inject an aliquot.

HPLC VARIABLES
Column: 250 × 4.6 5 μm cyano
Mobile phase: MeCN:100 mM NaH_2PO_4 20:80 adjusted to pH 4.2 with phosphoric acid
Flow rate: 0.8
Injection volume: 20
Detector: UV 195

CHROMATOGRAM
Retention time: 3.07

OTHER SUBSTANCES
Simultaneous: clavulanic acid, granisetron (UV 300)

KEY WORDS
stability-indicating; injections; saline

REFERENCE
Mayron,D.; Gennaro,A.R. Stability and compatibility of granisetron hydrochloride in i.v. solutions and oral liquids and during simulated Y-site injection with selected drugs, *Am.J.Health-Syst.Pharm.*, **1996**, *53*, 294–304.

SAMPLE
Matrix: milk
Sample preparation: Condition a Bond Elut C8 SPE cartridge with 5 mL MeOH and 5 mL water. 20 mL Milk + 1 mL 1 M oxalic acid, heat at 60° for 10 min, centrifuge for 10 min, remove the supernatant and add it to 20 mL water and 400 μL tributylamine, shake well, add to the SPE cartridge, wash with two 2.5 mL portions of water, elute with 2.5 mL MeOH. Evaporate the eluate to dryness under a stream of nitrogen, extract the residue with three 100 μL portions of 50 mM pH 6.0 potassium phosphate buffer, filter (0.2 μm), inject an aliquot of the filtrate. (Buffer was 545 mL 100 mM citric acid, 455 mL 200 mM Na_2HPO_4, and 74.4 g EDTA, adjust to pH 4.5 with ammonium hydroxide, make up to 2 L with water.)

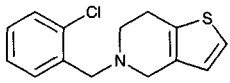
HPLC VARIABLES
Column: 250 × 4.6 10 μm Lichrosorb RP-8
Mobile phase: MeOH:50 mM pH 6.0 potassium phosphate buffer 35:65
Flow rate: 1
Injection volume: 200
Detector: UV 210 or Charm II assay

OTHER SUBSTANCES
Extracted: amoxicillin, cefadroxil
Simultaneous: ampicillin, ceftiofur, cephapirin, cloxacillin, dicloxacillin, nafcillin, oxacillin, penicillin G

KEY WORDS
SPE

REFERENCE
Zomer,E.; Quintana,J.; Saul,S.; Charm,S.E. LC-Receptograms: A method for identification and quantitation of β-lactams in milk by liquid chromatography with microbial receptor assay, *J.AOAC Int.*, **1995**, *78*, 1165–1172.

Ticlopidine



Molecular formula: $C_{14}H_{14}ClNS$
Molecular weight: 263.79
CAS Registry No.: 55142-85-3, 53885-35-1 (HCl)
Merck Index: 9569
Lednicer No.: 3 228

SAMPLE
Matrix: blood
Sample preparation: Condition a 1 mL Bond Elut C18 SPE cartridge (Varian) with 1 mL MeOH and 1 mL 10 mM NaOH. Add 50 μL 10 μg/mL IS in MeOH and 1 mL 1 M NaOH to 1 mL plasma, vortex, add to SPE cartridge, wash with 4 mL MeOH:10 mM NaOH 50:50, dry by sucking air through the cartridge, elute with 500 μL ethyl acetate, evaporate the eluate to dryness under a stream of nitrogen at 37°, dissolve the residue in 200 μL mobile phase, inject an aliquot.

HPLC VARIABLES
Guard column: 30 × 4 BST Rutin 10 C18 (Bio-Separation Technologies, Hungary)
Column: 250 × 4 BST Rutin 10 C18 BD (BST Rutin C18 is equivalent to Hypersil BDS C18)
Mobile phase: MeCN:MeOH:10 mM pH 4 NaH_2PO_4 buffer 40:40:20
Flow rate: 1
Injection volume: 50
Detector: UV 215

CHROMATOGRAM
Retention time: 11
Internal standard: 5-(2,4-o-dichlorobenzyl)(-4,5,6,7-tetrahydrotieno-[3,2-c] pyridine (18)
Limit of quantitation: 10 ng/mL

KEY WORDS
plasma; SPE

REFERENCE
Rona,K.; Ary,K.; Gachalyi,B.; Klebovich,I. Liquid chromatographic method for the determination of ticlopidine in human plasma, *J.Chromatogr.B*, **1997**, *693*, 393–398.

SAMPLE
Matrix: blood
Sample preparation: 250 μL Plasma + 250 μL water + 0.5 μg IS, vortex for 10 s, add to an Extrelut-1 SPE cartridge, let stand for 10 min, elute with 6.5 mL hexane. Evaporate the eluate to dryness under a stream of nitrogen at 35°, reconstitute the residue in 100 μL MeCN, inject a 50 μL aliquot.

HPLC VARIABLES
Column: μBondapak C18
Mobile phase: MeCN:10 mM pH 7.8 phosphate 30:70
Flow rate: 1.3
Injection volume: 50
Detector: UV 235

CHROMATOGRAM
Retention time: 7.7

Internal standard: 5-[2,4-(o-dichlorobenzyl)]-4,5,6,7-tetrahydrothieno[3,2-c]pyridine (PCR 2735) (11.2)
Limit of detection: 5 ng/mL
Limit of quantitation: 50 ng/mL

KEY WORDS
plasma; baboon; pharmacokinetics; SPE

REFERENCE
Arnoux,P.; Sales,Y.; Mandray,M.; Lechat,P.; Berger,Y.; Cano,J.-P. Quantitative high-performance liquid chromatographic, gas chromatographic, and gas chromatographic-mass spectrometric analysis of ticlopidine in baboon plasma after solid-phase extraction, *J.Pharm.Sci.*, **1991**, *80*, 1092–1095.

SAMPLE
Matrix: blood
Sample preparation: 1 mL Plasma + 20 μL 20 μg/mL imipramine hydrochloride in MeOH + 1 mL 500 mM pH 9 phosphate buffer, vortex briefly, add 7 mL n-heptane:isoamyl alcohol 98.5:1.5, shake on a rotating shaker at 32 rpm for 15 min, centrifuge at 1500 g for 5 min. Remove 6 mL of the organic layer and evaporate it to dryness under a stream of nitrogen at 60°, reconstitute the residue in 200 μL mobile phase, vortex for 10 s, centrifuge at 1500 g for 3 min, inject a 100 μL aliquot of the supernatant.

HPLC VARIABLES
Guard column: 20 × 4.6 5 μm Supelguard LC-8-DB (Supelco)
Column: 150 × 4.6 5 μm Supelcosil LC-8-DB
Mobile phase: MeCN:MeOH:buffer 20:25:55 (Buffer was 50 mM pH 3.0 KH_2PO_4 containing 0.2% triethylamine.)
Flow rate: 1
Injection volume: 100
Detector: UV 235

CHROMATOGRAM
Retention time: 7.6
Internal standard: imipramine hydrochloride (11.6)
Limit of quantitation: 5 ng/mL

KEY WORDS
plasma; pharmacokinetics

REFERENCE
Dal Bo,L.; Verga,F.; Marzo,A.; Ambrosoli,L.; Poli,A. Determination of ticlopidine in human plasma by high-performance liquid chromatography and ultraviolet absorbance detection, *J.Chromatogr.B*, **1995**, *665*, 404–409.

SAMPLE
Matrix: blood
Sample preparation: 2 mL Whole blood or plasma + 2 mL buffer + 5 mL chloroform:isopropanol:n-heptane 60:14:26, shake gently horizontally for 10 min, centrifuge at 2800 g for 10 min. Remove the lower organic layer and evaporate it to dryness under vacuum at 45°, reconstitute the residue in 100 μL mobile phase, centrifuge at 2800 g for 5 min, inject a 50 μL aliquot of the supernatant. (Buffer was saturated ammonium chloride solution 25% diluted with water, adjusted to pH 9.5 with 25% ammonia solution.)

HPLC VARIABLES
Column: 300 × 3.9 4 μm NovaPack C18
Mobile phase: MeOH:THF:buffer 65:5:30 (Buffer was 0.68 g/L (10 mM (sic)) KH_2PO_4 adjusted to pH 2.6 with concentrated orthophosphoric acid.) (At the end of each session wash the column with water for 1 h and MeOH for 1 h, re-equilibrate for 30 min.)
Column temperature: 30
Flow rate: 0.8
Injection volume: 50
Detector: UV 234

CHROMATOGRAM
Retention time: 4.91
Limit of detection: <120 ng/mL

KEY WORDS
whole blood; plasma; interferences may occur–compounds (all of which are extracted) elute in this order tenoxicam; iproniazid; methocarbamol; methotrexate; caffeine; nialamide; colchicine; cytarabine; benzoylecgonine; acetaminophen; diazoxide; dacarbazine; sulfinpyrazole; flumazenil; sulpride; morphine; atenolol; toloxatone; terbutaline; albuterol; phenobarbital; ranitidine; tiapride; phenol; chlormezanone; aspirin; metformin; ritodrine; codeine; sultopride; amisulpride; naltrexone; lisinopril; benzocaine; nizatidine; nalorphine; mephenesin; naloxone; sotalol; carteolol; procainamide; carbamazepine; bromazepam; nalbuphine; nadolol; procarbazine; dihydralazine; omeprazole; strychnine; acebutolol; glutethimide; chlorpropamide; glipizide; triazolam; prazosin; flunitrazepam; clonazepam; metoclopramide; melphalan; estazolam; tolbutamide; ephedrine; clonidine; pindolol; clobazam; minoxidil; disopyramide; nitrazepam; dextromethorphan; tofisopam; zopiclone; debrisoquine; sulindac; alprazolam; cycloguanil; lorazepam; methaqualone; ketamine; piroxicam; metoprolol; nifedipine; quinine; mephentermine; prilocaine; pentazocine; oxazepam; tiaprofenic acid; quinidine; celiprolol; ajmaline; yohimbine; lidocaine; secobarbital; viloxazine; mepivacaine; meperidine; doxylamine; labetalol; temazepam; amodiaquine; benperidol; droperidol; hydroxychloroquine; zolpidem; ketoprofen; alminoprofen; cicletanine; moclobemide; chloroquine; cocaine; timolol; nomifensine; ticlopidine; acenocoumarol; vindesine; mexiletine; dipyridamole; trazodone; pipamperone; pyrimethamine; benazepril; vincristine; metapramine; chlordiazepoxide; oxprenolol; warfarin; clorazepate; flecainide; phencyclidine; thiopental; fenfluramine; metipranolol; triprolidine; naproxen; buprenorphine; verapamil; buspirone; tianeptine; midazolam; bupivacaine; carbinoxamine; loprazolam; cetirizine; chlorpheniramine; moperone; cibenzoline; medifoxamine; astemizole; vinblastine; nicardipine; bisoprolol; diltiazem; glibornuride; reserpine; aconitine; nitrendipine; diazepam; mianserin; ramipril; haloperidol; tetracaine; alprenolol; acepromethazine; glibenclamide; chlorophenacinone; doxepin; nimodipine; diphenhydramine; cyclizine; histapyrrodine; phenylbutazone; demexiptiline; clozapine; proguanil; trifluperidol; medazepam; cyamemazine; bumadizone; suriclone; propranolol; acepromazine; dothiepin; dextromoramide; fenoprofen; dextropropoxyphene; loxapine; betaxolol; propafenone; promethazine; thioproperazine; methadone; amoxapine; quinupramine; opipramol; cyproheptadine; brompheniramine; mefenidramine; protriptyline; flurbiprofen; tetrazepam; zorubicin; prazepam; alimemazine; loperamide; imipramine; desipramine; levomepromazine; hydroxyzine; niflumic acid; penbutolol; fluvoxamine; pimozide; daunorubicin; indomethacin; maprotiline; tropatenine; etodolac; fluoxetine; amitriptyline; nortriptyline; tioclomarol; diclofenac; mefloquine; trimipramine; chlorambucil; lidoflazine; ibuprofen; floctafenine; alpidem; loratadine; chlorpromazine; clomipramine; carpipramine; thioridazine; fentiazac; clemastine; mefenamic acid; fluphenazine; prochlorperazine; penfluridol; bepridil; terfenadine; trifluoperazine

REFERENCE
Tracqui,A.; Kintz,P.; Mangin,P. Systematic toxicological analysis using HPLC/DAD, *J.Forensic Sci.*, **1995**, *40*, 254–262.

SAMPLE
Matrix: blood, urine
Sample preparation: Add 1 mL whole blood or urine to Toxi-Tube A (Toxi-Lab, Irvine CA), add 3 mL water, mix by gentle inversion for 5 min, centrifuge at 1500 g for 5 min. Remove the organic layer and evaporate it to dryness under a stream of nitrogen at 40°, reconstitute the residue with 50 μL MeCN:water 50:50, vortex for 10 s, centrifuge at 7500 g for 2 min, inject a 10 (urine) or 30 (blood) μL aliquot. (The detector wavelength shown is the wavelength of maximum absorbance. This will not necessarily be the optimal wavelength for the separation. Multiple wavelengths from 200-350 nm can be scanned using a diode-array detector. Otherwise, 220 nm may be a reasonable choice for initial work. Matrix may interfere.)

HPLC VARIABLES
Guard column: 20 mm long Symmetry C18
Column: 250 × 4.6 5 μm Symmetry C8 (Waters)
Mobile phase: Gradient. A was 50 mM pH 3.8 sodium phosphate buffer. B was MeCN. A:B 85:15 for 6.5 min, 65:35 for 18.5 min, 20:80 for 3 min (step gradient), re-equilibrate at initial conditions for 7 min.
Column temperature: 30

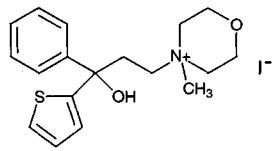
Flow rate: 1 for 6.5 min, to 1.5 over 18.5 min, maintain at 1.5 for 3 min (re-equilibrate at 1.5 mL/min)
Injection volume: 10-30
Detector: UV 200.5

CHROMATOGRAM
Retention time: 13.813

KEY WORDS
whole blood

REFERENCE
Gaillard,Y.; Pépin,G. Use of high-performance liquid chromatography with photodiode-array UV detection for the creation of a 600-compound library. Application to forensic toxicology, *J.Chromatogr.A*, **1997**, *763*, 149–163.

Tiemonium iodide



Molecular formula: $C_{18}H_{24}INO_2S$
Molecular weight: 445.36
CAS Registry No.: 144-12-7
Merck Index: 9571

SAMPLE
Matrix: blood, urine
Sample preparation: Add 1 mL whole blood or urine to Toxi-Tube A (Toxi-Lab, Irvine CA), add 3 mL water, mix by gentle inversion for 5 min, centrifuge at 1500 g for 5 min. Remove the organic layer and evaporate it to dryness under a stream of nitrogen at 40°, reconstitute the residue with 50 µL MeCN:water 50:50, vortex for 10 s, centrifuge at 7500 g for 2 min, inject a 10 (urine) or 30 (blood) µL aliquot. (The detector wavelength shown is the wavelength of maximum absorbance. This will not necessarily be the optimal wavelength for the separation. Multiple wavelengths from 200-350 nm can be scanned using a diode-array detector. Otherwise, 220 nm may be a reasonable choice for initial work. Matrix may interfere.)

HPLC VARIABLES
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Column temperature: 30
Flow rate: 1 for 6.5 min, to 1.5 over 18.5 min, maintain at 1.5 for 3 min (re-equilibrate at 1.5 mL/min)
Injection volume: 10-30
Detector: UV 200.5

CHROMATOGRAM
Retention time: 11.795

KEY WORDS
whole blood

REFERENCE
Gaillard,Y.; Pépin,G. Use of high-performance liquid chromatography with photodiode-array UV detection for the creation of a 600-compound library. Application to forensic toxicology, *J.Chromatogr.A*, **1997**, *763*, 149–163.